The Journal

OF THE

American Medical Association

EDITED FOR THE ASSOCIATION UNDER THE DIRECTION OF THE BOARD OF TRUSTEES BY

JOHN H. TALBOTT, M.D.

VOLUME 172

OFFICIALS OF THE AMERICAN MEDICAL ASSOCIATION—1959-1960

Headquarters of the Association, 535 N. Dearborn St., Chicago 10

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JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE DEPARTMENT, JANUARY-APRIL 1960

Abstracts have been made of important articles in the following journals in the Current Medical Literature Department of The Journal during the past four months. Any of the journals, except those starred, will be lent by the Library of the American Medical Association to individuals in Continental United States and Canada who subscribe to its scientific periodicals and to members of the American Medical Association and its student organization. No charge is made to members, but the fee for other borrowers is 15 cents in stamps for each periodical. Three journals may be borrowed at a time for a period not exceeding five days. Thus most of these journals are accessible to the general practitioner.

*A. M. A. Archives of Dermatology. Chicago.
*A. M. A. Archives of General Psychiatry. Chicago.
*A. M. A. Archives of Industrial Health. Chicago.
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*A. M. A. Journal of Diseases of Children. Chicago.
Acta chirurgica scandinavica. Stockholm.
Acta haematologica. Basel.
Acta medica scandinavica. Stockholm.
Acta paediatrica belgica. Brussels.
Acta tuberculosea scandinavica. Copenhagen.
American Heart Journal. St. Louis.
American Journal of Cardiology. New York.
American Journal of Clinical Pathology. Baltimore.
American Journal of Gastroenterology. New York.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Medicine. New York.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. Chicago.
American Journal of Pathology. Ann Arbor, Mich.
American Journal of Public Health and the Nation's Health. Albany, N. Y.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Review of Respiratory Diseases.
American Surgeon. Baltimore.
Anales de cirurgía. Rosario.
Anales de la Facultad de medicina. Montevideo.
Anesthesiology. Philadelphia.
Angiology. Baltimore.
Annales chirurgiae et gynaecologiae Fenniae. Helsinki.
Annals of Allergy. St. Paul.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otology, Rhinology and Laryngology. St. Louis.
Annales paediatrici. Basel.
Annales
Annals o
Annals o
Antibioti New York.
Archiv f
Archiv f
Archiv f heiten vereinigt mit Zeitschrift
für di chiatrie. Heidelberg.
Archives m.
Archives françaises de pédiatrie. Paris.
Archives des maladies de l'appareil digestif et des maladies de la nutrition. Paris.
Archives des maladies du coeur et des vaisseaux. Paris.
Archives of Pediatrics. New York.
Archives Rehabilitation. Chicago.
Archivos de México. México, D. F.
Archivum m.
Arquivos min rizonte.
Arquivos de
Australasian
Beiträge zur
Beiträge zur
Bibliotek for laeger. Copenhagen, Denmark.
a. Lisbon.
Rico. Santurce.
Brain. London.
British Heart Journal. London.
British Journal of Diseases of the Chest. London.
British Journal of Ophthalmology. London.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Urology. Edinburgh.
British Medical Journal. London.
California Medicine. San Francisco.
Canadian Journal of Public Health. Toronto.
Canadian Journal of Surgery. Toronto.
Canadian Medical Association Journal. Montreal.
Cancer. Philadelphia.
Chirurg. Berlin.
La chirurgia toracica. Rome.
v Haven.
Stuttgart.
Diseases of the Chest. Chicago.
Diseases of the Colon and Rectum. Philadelphia.
Electroencephalography and Clinical Neur

Gaceta médica de México. México, D. F.
Gastroenterology. Baltimore.
German Medical Monthly. Stuttgart.
Harefuah. Tel-Aviv, Israel.
Hawaii Medical Journal and Inter-Island Nurses' Bulletin. Honolulu.
Helvetica medica acta. Basel.
Helvetica paediatrica acta. Basel.
Hospital. Rio de Janeiro.
Industrial Medicine and Surgery. Chicago.
International Journal of Leprosy. New Orleans.
Irish Journal of Medical Science. Dublin.
Journal of the American Medical Women's Association. New York.
Journal of Bone and Joint Surgery. Boston and London.
Journal of Chronic Diseases. St. Louis.
Journal of Clinical Endocrinology and Metabolism. Springfield, Ill.
Journal of Clinical Investigation. New Haven.
Journal of Clinical Pathology. London.
Journal of the Florida Medical Association. Jacksonville.
Journal of Infectious Diseases. Chicago.
Journal of International College of Surgeons. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of the Kentucky State Medical Association. Louisville.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal-Lancet. Minneapolis.
Journal of Laryngology and Otology. London.
Journal of the Louisiana State Medical Society. New Orleans.
Journal of the Maine Medical Association. Portland.
The Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal of the Mississippi Medical Association. Fulton, Mo.
Journal of the National Cancer Institute. Washington, D. C.
Journal of the National Medical Association. New York.
Journal of Neurology, Neurosurgery and Psychiatry. London.
Journal of Neurosurgery. Chicago.
Journal of Obstetrics and Gynaecology of the British Empire. London.
Journal of Oklahoma State Medical Association. Oklahoma City.
Journal of Pediatrics. St. Louis.
Journal of South Carolina Medical Association. Florence.
Journal of Tennessee State Medical Association. Nashville.
Journal of Thoracic Surgery. St. Louis.
Journal of Urology. Baltimore.
Klinische Monatsblätter für Augenheilkunde und für augenärztliche Fortbildung. Stuttgart.
Klinische Wochenschrift. Berlin.
Lancet. London.
Maandschrift voor kindergeneeskunde. Leiden.
Medical Journal of Australia. Sydney.
Medicina clinica. Barcelona.
Medicine. Baltimore.
Minerva cardioangiologica. Turin.
Minerva chirurgica. Turin.
Monatsschrift für Kinderheilkunde. Berlin.
Münchener medizinische Wochenschrift. Munich.
voor geneeskunde. Amsterdam.
Medicine. Boston.
of Medicine. New York.
The New Zealand Medical Journal. Wellington.
Nordisk medicin. Stockholm.
North Carolina Medical Journal. Winston-Salem
Northwest Medicine. Seattle.
Obstetricia y ginecología latino-american
Obstetrics and Gynecology. New York.
Ohio State Medical Journal. C
Pediatrics. Springfield, Ill.
Pennsylvania Medical Jo
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tablets, for oral dosage of 10 mg.
of 1 cc. for intramuscular injection,
containing 25 mg. of the drug in sesame oil and
cent of benzyl alcohol by volume.

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1. Ibarra, J. D., Jr.: Osteoporosis, Texas J. Med. 52:20 (Jan.) 1956.
2. Spencer, H.; Berger, E.; Charles, M. L.; Gottesman, E. D., and Laszlo, D.: Metabolic Effects of 17-Ethyl-19-Nortestosterone in Man, J. Clin. Endocrinol. 17:975 (Aug.) 1957.
3. Snapper, I.: Bone Diseases in Medical Practice, New York, Grune & Stratton, Inc., 1957, p. 18.
4. Spurr, C. L.; Curd, G. W., Jr., and Moyer, J. H.: Newer Anti-Inf matory Steroids: Mechanisms of Action and Therapeutic Appl GP 15:105 (May) 1957.
5. Editorial: Tissue Building and Protein Anabolizers, Brit. M. J. 2: (Sept 27) 1958.

Revista paulista de medicina. São Paulo.
Revue française d'études cliniques et biologiques. Paris.
Revue de la tuberculose. Paris.
Rheumatism. London.
Riforma medica. Naples.
Rocky Mountain Medical Journal. Denver.
Schweizerische medizinische Wochenschrift. Basel.
Science. Washington, D. C.
Scottish Medical Journal. Glasgow.
Semaine des hôpitaux de Paris. Paris.
Semana médica. Buenos Aires.
Settimana medica. Florence.
Southern Medical Journal. Birmingham, Ala.
Southwestern Medicine. El Paso.
Strahlentherapie. Munich.
Surgery, Gynecology and Obstetrics. Chicago.
Surgery. St. Louis.
Texas State Journal of Medicine. Austin.
Thorax. London.
Thoraxchirurgie. Stuttgart.
Tidsskrift for den norske laegeforening. Oslo.
Tórax. Montevideo.
Tuberkulosearzt. Stuttgart.
Tumori. Milan.
Ugeskrift for laeger. Copenhagen.
Union médicale du Canada. Montreal.
Vestnik khirur. [illegible]
West Virginia [illegible]
Wiener klinisc [illegible]
Wiener Zeitschrift für innere Medizin und ihre Grenzgebiete. Vienna.
Wisconsin Medical Journal. Madison.
Yale Journal of Biology and Medicine. New Haven.
Zeitschrift für Kinderheilkunde. Berlin.
Zeitschrift für Orthopädie und ihre Grenzgebiete. Stuttgart.
Zeitschrift für Urologie. Leipzig.

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*Cannot be lent.

WASHINGTON NEWS

Tax Cut Prospects . .
Penicillin In Milk . .
Lipstick Color Law . .
Miscellany . .

MAJOR TAX CUT THIS YEAR UNLIKELY

Chairman Wilbur Mills (D., Ark.) of the House Ways and Means Committee virtually ruled out the possibility of a sizeable tax reduction this year. At the close of committee hearings on proposals to broaden the tax base and therefore make a tax cut possible without affecting revenues, Mills said it would be "at least until 1961" before the staffs of the committee and the Treasury Department could present a tax revision plan to the committee.

Some 175 tax experts, economists, and spokesmen for national organizations, including the American Medical Association, proposed various tax changes during the committee's five weeks of hearings before the Congressional session started. In a statement presented the Ways and Means Committee, Dr. F. J. L. Blasingame, A. M. A. Executive Vice-president, said a partial solution of the economic problems of the elderly would be further tax deductions. He also said graduated federal income tax rates are especially unfair to professional people who derive their income from services because they are not granted special treatments afforded other types of business income.

Meanwhile, Social Security taxes, at the first of the year increased an additional 20%, the fifth hike in the last six years. The increased tax load on employers and workers was expected to total about 2 billion dollars. By 1969 the Social Security tax rate is slated under already-passed legislation to be 80% higher than in 1959. Any further changes in the system such as financing health care for the aged would, of course, cause the tax rates to go even higher, an estimated 2 billion dollars extra annually.

FEDERAL CAMPAIGN AGAINST PENICILLIN IN MILK

The Food and Drug Administration annc senile
that it is stepping up a program to elimabolic reactic
of penicillin in interstate shipmentis. An added advan-
eoporosis is that the drug
cium and so serves both the pri-
eoblasts and the secondary process of
of the antibiotic, used in the treatment of some cattle diseases, might cause reactions in persons sensitive to penicillin.

The FDA noted that there has been a significant decrease in penicillin-contaminated milk and that the industry has cooperated fully with the government in an educational campaign for dairy farmers. The milk of cows treated with penicillin may contain antibiotic residues up to 72 hours after the latest treatment.

Penicillin and other antibiotic drugs used to treat mastitis in cows must bear labels stating that milk from treated cows must not be used for human consumption for at least 72 hours.

Since the start of the educational campaign four years ago, the percentage of samples shown to contain penicillin have dropped from 11.6 to 3.7 this year.

However, FDA Commissioner George P. Larrick declared "the educational effort alone is not enough. The contaminants cannot be tolerated in the milk supply. We will have to take legal actions where necessary."

Meanwhile, federal scientists said that the danger of milk contamination by pesticides such as DDT is being reduced. They made the statement after publication of a 1958 government survey showing that some milk in 11 cities across the nation was tainted with pesticides containing chlorine.

LIPSTICK COLOR LAW CHANGE URGED

John L. Harvey, Deputy Commissioner of the Food and Drug Administration, declared that the present law affecting lipstick coal-tar dyes is "unrealistic" and should be changed. Noting that the cosmetics industry has requested hearings in early January on FDA's decision to ban 17 of the coal-tar dyes used in lipstick, Harvey said the prese
"regards colors as either 'harmless' in ac-
they are allowed in any quanti courses of
in which case they are no three months, but
"No substance is comr of one month.
"so we have colors al
cosmetics without olets, for oral dosage, of 10 mg.
may cause h of 1 cc. for intramuscular injection,
The ntaining 25 mg. of the drug in sesame oil and
wi cent of benzyl alcohol by volume.

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1. Ibarra, J. D., Jr.: Osteoporosis, Texas J. Med. 52:20 (Jan.) 1956.
2. Spencer, H.; Berger, E.; Charles, M. L.; Gottesman, E. D., and Laszlo, D.: Metabolic Effects of 17-Ethyl-19-Nortestosterone in Man, J. Clin. Endocrinol. 17:975 (Aug.) 1957.
3. Snapper, I.: Bone Diseases in Medical Practice, New York, Grune & Stratton, Inc., 1957, p. 18.
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5. Editorial: Tissue Building and Protein Anabolizers, Brit. M. J. 2:785 (Sept. 27) 1958.

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A delightful booklet where babies do the talking through pictures and captions. 36 pages, 25 cents

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Tells how to prevent accidents from choking and what to do if they happen. by Chevalier Jackson and Chevalier L. Jackson. 24 pages, 15 cents

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Including sleep disturbances, eating problems, stubbornness, bladder control. by H. M. Jahr, 16 pages, 20 cents

MISCELLANY

The National Science Foundation estimated that total spending for scientific research and development in this country will reach an all-time high of 12 billion dollars during the fiscal year that ends next June 30. The foundation estimated that expenditures by the federal government will rise from 970 million dollars for the 1954 fiscal year to 1.78 billion dollars for 1959-1960; by colleges and universities from 450 million to 1 billion dollars, and by other nonprofit institutions, such as philanthropic and health agencies, from 100 million to 250 million dollars.

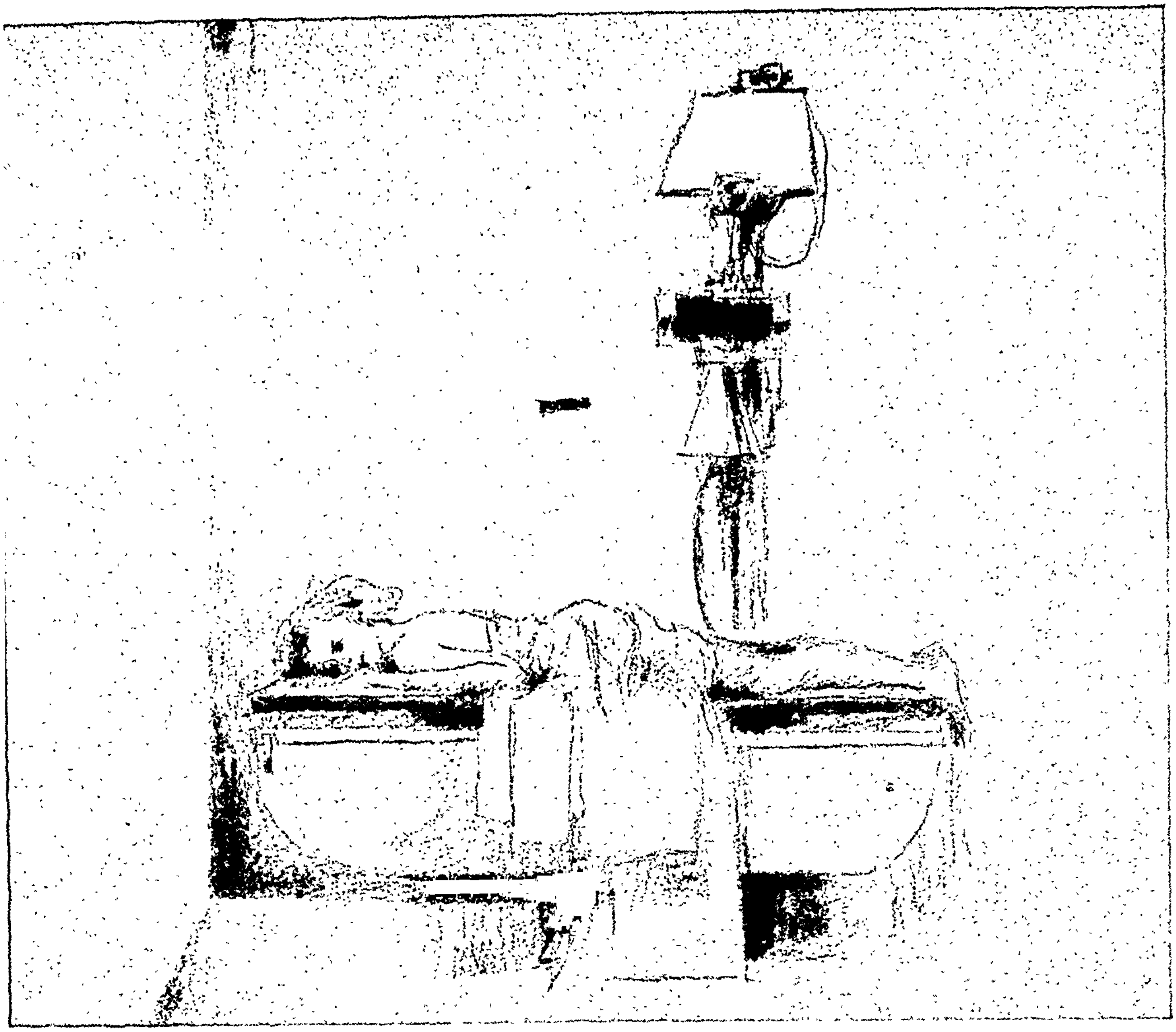
The Internal Revenue Service said that it will continue to follow the policy that only that portion of an insurance policy premium properly attributable to the coverage for medical expenses may be deductible as an expense for medical care. The agency made the statement after a U. S. Court of Appeals ruling that the entire premium is deductible on a policy providing indemnity for accidental loss of life, limb, sight, and time and also providing for reimbursement of medical expenses resulting from nondisabling accidents. The disputed interpretations may eventually have to be settled by the U. S. Tax Court.

The government plans to start compiling national data next year on malformations at birth, in an effort to gather more medical and statistical knowledge, including the possible hereditary effects of radiation. The program by the Office of Vital Statistics will at first be a compilation of congenital malformations that are now required to be reported on birth certificates in 40 states. It was planned to expand the program later to include more detailed information.

The Atomic Energy Commission said that some of a group of about 600 special navigational watches imported by the American Rolex firm contained radioactive strontium-90 and constituted a possible health threat. The company asked its distributors to notify purchasers of the watch so that they could be returned for inspection. The AEC said that the probability is very small that exposure from normal wear would result in appreciable damage, but "such exposures to radiation from a wrist watch should not be permitted."

CHANGE OF ADDRESS

If you change your address please notify THE JOURNAL at least six weeks before the change is made. Include the address label clipped from your latest copy of THE JOURNAL, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Number in your new address.



Nilevar® Combats Osteoporosis in Menopause or Hypercorticism

Since osteoporosis is a disease not of calcium deficiency but primarily of deficient formation of the protein bone matrix[1], the protein-building action of Nilevar (brand of norethandrolone) provides a rational and highly useful means of promoting osteogenesis.

Typically, subjective symptoms such as backache disappear promptly in osteoporotic patients treated with Nilevar. Objectively, the anabolic effects of the drug may be measured in the lessened excretion of nitrogen, calcium, potassium and phosphorus.

These actions appear to be equally effective[2-5] whether the osteoporosis originates in the postmenopausal or senile metabolic deficiencies of women or in the catabolic reaction to extended treatment with corticosteroids. An added advantage to the use of Nilevar in osteoporosis is that the drug promotes a retention of calcium and so serves both the primary work of the osteoblasts and the secondary process of recalcification.

An initial adult dosage of 10 mg. three times a day may be continued for two or three weeks and then reduced in accordance with the response of the patient. Single courses of continuous treatment should not exceed three months, but may be resumed after a rest period of one month.

Nilevar is supplied as tablets, for oral dosage, of 10 mg. each and as ampuls of 1 cc. for intramuscular injection, each ampul containing 25 mg. of the drug in sesame oil and 10 per cent of benzyl alcohol by volume.

G. D. SEARLE & CO. Research in the Service of Medicine.

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1. Ibarra, J. D., Jr.: Osteoporosis, Texas J. Med. 52:20 (Jan.) 1956.
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5. *Editorial: Tissue Building and Protein Anabolizers,* Brit. M. J. 2:785 (Sept. 27) 1958.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, North Carolina Chapter, Hotel Barringer, Charlotte, N. C., Feb. 26-27. For information write Dr. Alexander Webb Jr., 201 Bryan Bldg., Cameron Village, Raleigh, N. C.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

American Academy of General Practice, Philadelphia, Mar. 18-24. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Mo., Executive Director.

American Association for the History of Medicine, Inc., Charleston, S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Institution, Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadmoor, Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Portland Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, New Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. of Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. 30. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Treasurer.

American Laryngological Association, Deauville Hotel, Miami Beach, Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Technology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Society, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Fla., Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneapolis 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, Montreal, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N. Y., Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Rico, Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory University, Atlanta 22, Ga., Secretary.

Intermountain Pediatric Society, Stardust Hotel, Las Vegas, Nev., Mar. 28-29. Dr. Joseph R. Newton, 2000 S. 9th East, Salt Lake City, Utah, Publicity Chairman.

Missouri State Medical Association, Sheraton-Jefferson Hotel, St. Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Louis 3, Executive Secretary.

National Health Council, National Health Forum, Miami, Fla., Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, Executive Director.

National Multiple Sclerosis Society, New York City, Mar. 8. Mr. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. 30-Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore 1, Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, New Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., New Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, Mar. 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Executive Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev., Mar. 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma City, Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Semmes Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jackson St., Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla., Apr. 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Executive Secretary.

American Association of Anatomists, Statler-Hilton, New York City, Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Medicine, Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, Chicago, Apr. 11-15. Dr. Calderon Howe, Columbia Univ. College of Physicians and Surgeons, New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, Hotel Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman, Dept. of Pathology, L. S. U. School of Medicine, New Orleans, La., Secretary.

American Association of Railway Surgeons, Drake Hotel, Chicago, Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Executive Secretary.

American College of Obstetricians and Gynecologists, Netherland Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardson, 79 W. Monroe St., Chicago 3, Executive Secretary.

American College of Physicians, Mark Hopkins & Fairmont, San Francisco, Apr. 4-9. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

American College of Surgeons, Sectional Meeting, Hotel Leamington, Minneapolis, Apr. 11-13. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Kahler Hotel, Rochester, Minn., Apr. 14. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Dermatological Association, Inc., Boca Raton Hotel, Boca Raton, Fla., Apr. 8-12. Dr. Wiley M. Sams, 308 Ingraham Bldg., Miami 32, Fla., Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. Daggs, D.Sc., 9650 Wisconsin Ave., Washington 14, D. C., Executive Secretary.

American Proctologic Society, Shamrock Hilton Hotel, Houston, Texas, Apr. 25-27. Dr. Norman D. Nigro, 10 Peterboro, Detroit 1, Secretary.

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MULTIPHASIC SCREENING OF THE WELL PATIENT

TWELVE-YEAR EXPERIENCE OF THE TULANE UNIVERSITY CANCER DETECTION CLINIC

Joseph E. Schenthal, M.D., New Orleans

A study was made of the health status of persons who considered themselves free from disease. Multiphasic examinations carried out in 10,709 apparently healthy subjects showed that 92% had either organic or functional disease. Malignancy was detected in 77 (0.72%), and all those questioned about it stated they had been unaware of it. Cardiopathy was found in 804 examinees, the most frequent form (26.5%) being myocardial disease. The data indicated the importance of systematic health examinations and suggested ways of establishing a base line of what to expect in various age groups.

DURING the last 15 years there has been increasing awareness that an understanding of the well and asymptomatic person can be of considerable value to the clinician in the control of the natural course of pathological physiology and disease. This interest also has indicated that considerably less may be known about the total well person than about the ill patient.[1] As a result there has been a demand for more knowledge about the well person, which has, in part, been related to the current program for the control of both degenerative and malignant disease. With heart, vascular, and malignant diseases as leading causes of death, attention has been concentrated on the detection and treatment of these conditions early in the natural course of development.[2] Another factor has been the increased demand of both industry and the armed services during and after World War II for active maintenance of health in the physically fit person.[3] Limited screening examinations in these fields have indicated that a multiphasic examination will uncover disease and abnormalities, but there have been few data which would give the clinician a base line of what to anticipate of his total patient at any one instant. The Tulane University Cancer Detection Clinic has been concerned with the status of the total, well patient, [illegible] emphasis on the extent and types of disorders which the ph[illegible] may anticipate finding on an initial examination of an asymptomatic [illegible]ding to the Poisson [illegible]ce of isolated events in a

History of Multiphasic [illegible]

The use of the [illegible] myocardial infarction, detected [illegible]vestigative [illegible]mation in two persons; retinopathy [illegible] edema in one person on his second exam[illegible]ion; detachment of the retina, in one person on initial examination; carcinoma of the colon, in one person on second examination; malignant degenera-

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From the departments of medicine and preventive [illegible] tion clinic was founded at the New York Infirmary by Dr. Elise L'Esperance in 1937. It was followed in 1938 by a second at the Women's Medical College of Pennsylvania: a third was founded by Dr. L'Esperance at the Memorial Hospital in New York City. These were the first to offer comprehensive examinations to asymptomatic adults and, after an interruption by World War II, were followed, after 1945, by the organization of many clinics in the United States. The Tulane University Cancer Detection Clinic began operation in March, 1946.[4] By 1949 there were 250 clinics in the United States, varying markedly in size and scope of activities. These have decreased in number to about 200 at the time of writing.[5] Practically all have been used as demonstration units for the evaluation of old and new methods of examination for the early detection of malignant and nonmalignant disease. In the case of the clinic with an extensive scope, including multiphasic screening of the total well person, this has given extensive information on the value and technique of an initial or periodic examination.[6]

Age Distribution of 10,709 Consecutive Examinees in Multiphasic Screening of Well Patients

Age, Yr.	Examinees, No.	Percentage
10-19	60	0.6
20-29	1,261	11.8
30-39	3,187	29.8
40-49	3,116	29.0
50-59	2,000	18.7
60-69	856	8.0
70-79	216	2.0
80-89	13	0.1

Methods and Procedures

Participating in this trend in medicine, a multiphasic screening examination of the total person as a single, initial procedure, such as could be carried out in a physician's office, was organized and carried out by the Tulane University Cancer Detection Clinic. The medical staff of the clinic consisted of members of the faculty of the Tulane Medical School and included three to four internists, two gynecologists, one cytologist, one clinical pathologist and his staff of medical technicians, one roentgenologist, and one nurse. A medical director, secretary, and clerk administer the clinic operation.

This clinic has functioned in the Tulane Medical School (Hutchinson Memorial Clinic) by making use of the facilities of the school and surveying the examinees during a two-hour period twice a week. [illegible] the examination included procedures considered appeared [illegible] a general survey. Diagnostic measures in whom three [illegible]amination, other than those car- single examination [illegible] operation, were expected to of the diseases [illegible] [illegible]wn chosen phy- cal or patholog[illegible]. The actual ex- illustrative examples are shown in [illegible]ed medical

In attempting to identify possible sources [illegible]logist in the data dealing with this aspect of the study, we have considered the habits of physicians in recording diagnoses. While one physician might tend to

proctosigmoidoscopy (if acceptable to the examinee). Laboratory examination included determination of hematocrit, hemoglobin level, white blood cell count, serologic test for syphilis, urinalysis, and x-ray of the chest. Cytological examinations for uterine cancer were made routinely from 1946 to 1951, and from July, 1957, to the time of writing.

The examinee accepted by the clinic was an apparently well and asymptomatic person who was not under treatment for illness and who had not been surveyed by a physician in the preceding six months. The examinees included all applicants who belonged to the preceding category, with the understanding that all findings were to be reported to the physicians of their choice for further evaluation, indicated treatment, and further periodic examinations. A small percentage of reexaminations were made during the first three years of operation of the clinic. The vast majority of examinees were located in the Greater Metropolitan New Orleans area and became informed of the clinic through contact with former examinees, no publicity being conducted by the clinic.

The final report of the examination was mailed to a physician (either to a private physician or to a public clinic), as designated by the examinee. The person concerned was advised to contact his or her physician, who would evaluate the report and carry out additional diagnostic measures and treatment if indicated. Further routine, periodic health inventories were to be carried out by the examinee's physician, the examinee being ineligible to return to the clinic for 10 years. A follow-up report was requested from the physician after an appropriate interval.

Results

The examinees included a total of 10,709 apparently well and asymptomatic adults examined during the 12-year period, 1946 to 1958, of whom 97% were well patients of private physicians and 3% indigent, well patients of public clinics. Of the total, 24.5% were males and 7.6% were Negroes. The subjects represented all socioeconomic levels of the community and many occupations, the vast majority being gainfully employed or homemakers. The majority of the examinees (59%) were between the ages of 30 and 49 years (see table). There was decreased attendance by the age group 50 to 59 (18.7%) and less by the age group 20-29 (11.7%). A decrease in attendance was exhibited after the age of 60 years. There was very little attendance of persons below the age of 20 years and above the age of 79 years. The clinical findings indicated that disease or abnormalities of varying significance were present in all but 8.2% of the total number of examinees.

Malignancies were detected in 77 (0.72%) of the total examined. This is considered a minimal quantity related to 64% of follow-up reports obtained exa[illegible]he examinees' physicians. They were present [illegible] all age groups, with 25% occurring in persons between 20 and 49 years of age. These malignancies included cancer of the thyroid (1), tonsil (1), larynx (2), breast (17), lung (4), stomach (1), rectum (4), sigmoid colon (5), ovary (2), uterine cervix (15), uterine endometrium (1), kidney (1), bladder (1), prostate (1), testis (1), and skin (20).

Conditions or benign neoplasms of premalignant significance occurred in 444 examinees (4.1%). These included ductal papillomas (5) and comedoadenosis (1) of the breast. Leukoplakia was noted of the buccal mucosa (41), lip (19), tongue (2), nipple (3), cervix (32), vagina (1), and vulva (28). Particular pigmented nevi were singled out in 94 persons, and skin keratosis in 128. Single adenomas of the thyroid (35), testicular atrophy (17), and rectal polyps (38) also warranted consideration in this group.

Between 1.5 and 3% of the group examined were considered to have strongly suggestive clinical evidence of malignancy and required further diagnostic evaluation for the definite exclusion of malignancy.

Significant nonmalignant abnormalities were noted in 91% of the examinees. The vast majority of these conditions was determined objectively by the examining physician, although a proportion of such abnormalities as the gastrointestinal disease that had been revealed was related to the interpretation of the symptomatology. In addition, the etiology of certain types of disease could not in some instances, be determined on the basis of the screening examination and the follow-up reports, as exemplified by the myocardial disease of undetermined etiology (fig. 1). The heart disease, as well as the vascular disease found (fig. 2), [illegible] scattered throughout the age groups; a [illegible] proportion of this appeared to be sufficiently early in its natural course to merit close consideration relative to reversibility and prevention of sequelae. [illegible]arily to

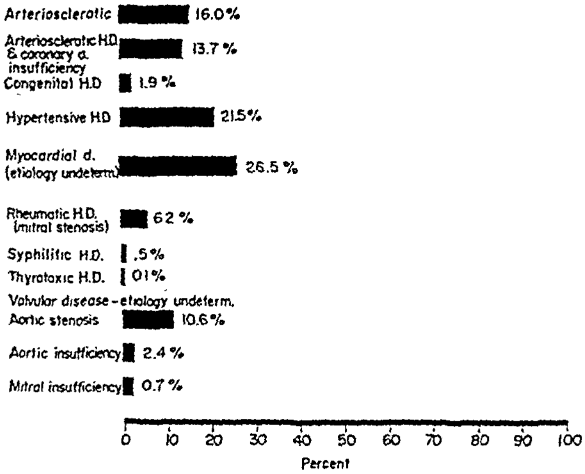

Fig. 1.—Percentage distribution of 804 cases of heart disease detected in single screening examination of each of 10,709 apparently well examinees.

Gynecologic abnormalities amounted to 65.3%, which is considered a minimal figure and, in this particular group, difficult to ascertain because of the multiple findings per examinee. In this group diseases of the cervix predominated (49%), a far smaller proportion of disease involving the adnexa (5.4%), body of the uterus (4.7%), and vagina (5.35%). The latter was primarily vaginitis.

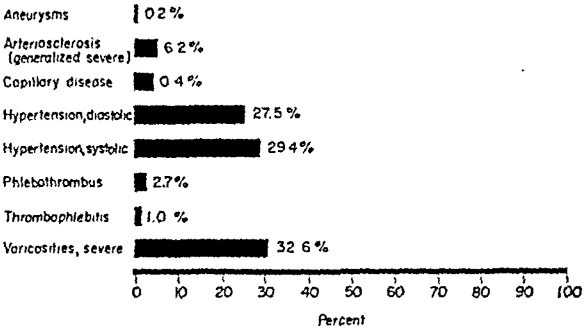

Fig. 2.—Percentage distribution of 1,302 cases of vascular disease detected in single screening examination of each of 10,709 apparently well examinees.

Laboratory findings requiring further evaluation (38.6%) was the next largest group of significance. Of the total group of examinees, anemia (less than 11 Gm. of hemoglobin) was present in 1.9%, while albuminuria (10.9%), renal casts (10.8%), and glycosuria (11.5%) were of much higher incidence.

Gastrointestinal disorders (21.3%) made up the third-largest group of nonmalignant disease, much of this depending on the symptoms elicited by a scrutinizing and probing history. While most of the conditions in this group, such as hemorrhoids (74.4%) were of little significance, disease or abnormal function of the stomach and duodenum was detected in 13.3%, of the colon in 5%, and of the rectum in 5.2%.

Genitourinary tract disease (6.2%) was distributed between types of chronic nephritis, lower urinary tract inflammatory disease, and prostatitis. Also among the classifications of lower incidence were musculoskeletal disorders (5.0%), including rheumatoid arthritis and osteoarthritis, and postural abnormalities. Respiratory tract disease (31.6%) was small in percentage but of significance as to the type of involvement detected, namely, chronic asthma, bronchitis, bronchiectasis, pneumonitis, an[illegible] active tuberculosis (0.3% of the total numb[illegible] examinees).

Of the total of 10,709 examinees [illegible] tive examinees were further e[illegible] awareness or knowledg[illegible] 30 60 & OVER disease processes [illegible] new diagnosis made on first examtion. All of th[illegible] seriousness of disease. practicall[illegible] number of persons with more than their share of disease of all types, suggests a pattern of "disease proneness," the possible causes of which we cannot assess.

of eye, ear, nose, and throat disease and 57% of genitourinary tract pathology. Not to be overlooked was asymptomatic pathology about which the examinee had been informed in the past and for which evaluation and treatment were indicated. While this was considered as disease which was known to the examinee, awareness of a good proportion of this had been repressed and was brought into focus by the history-taking procedures.

Comment

Multiphasic examinations of 10,709 examinees indicated that practically all (92%) of these subjects, who considered themselves well and declared themselves asymptomatic, had disease or pathological physiology which was amenable to diagnosis and treatment. Much of this disease was in the early stages of the natural course of the disease process.[1a] Those persons who were motivated to be examined were, to a large extent, in their productive years, either as wage earners or as homemakers. It is probable that a small number denied symptoms of illness in order to obtain examinations. Likewise, it is difficult at this time to estimate the total number of emotionally disturbed subjects, in excess of the 2.9% who were clinically diagnosed as such, who presented themselves on the basis of significant anxiety.

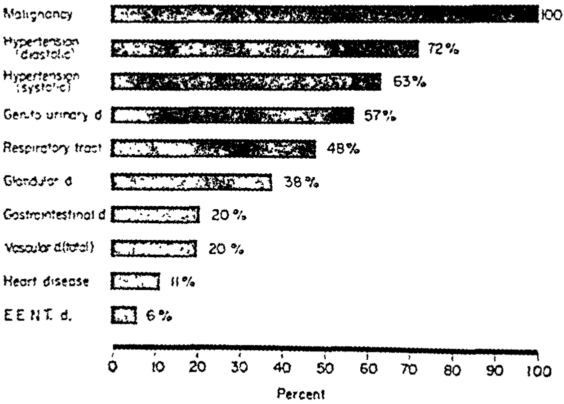

Fig. 3.—Figure shows ten of the major disease processes detected among 2,850 consecutive, apparently well persons and the percentage of examinees, in each of these categories, to whom the disease was unknown.

It is anticipated that recent developments in
tiphasic screening will facilitate the search for
elation of mass medical data to determine
nificance of the various factors enter-
rabiestion to be medically examined,
from the subclinical illness, public
may be as freq inventories, or a com-
was found to persist motivating at a
infected bats and was occ the disease.
that brown adipose tissue provi stent
as reservoirs for this agent in nature.—
R. Allen, and C. Wallis, Studies on the
Bats, *The Journal of Experimental Medicine*, Sept.

of the total yield of pathology in the younger age groups, who exhibited exceptional interest in periodic health examinations. The basic technique of the examination is similar to that which can be carried out by every physician.

Recent studies made in this clinic indicate the feasibility of making use of the electronic digital computer as an aid in clinical evaluation. The routine clinical application of data obtained from an electronic processing apparatus may be expected to give more information about multiphasic screening in relation to disease patterns in the near future.

Summary

We have presented the history of the new trend whereby the physician is increasingly concerned with the maintenance of health in his well patient. Clinical data as determined by the Tulane University Cancer Detection Clinic may be used as a base line of the type and extent of the disease and abnormalities that exist in apparently well and asymptomatic persons.

1430 Tulane Ave. (12).

The Tulane University Cancer Detection Clinic has been aided by yearly grants from the Louisiana division of the American Cancer Society from 1946 to 1958 and from the Louisiana State Department of Health from 1951 to 1958.

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PERIODIC HEALTH EXAMINATION

NATURE AND DISTRIBUTION OF NEWLY DISCOVERED DISEASE IN EXECUTIVES

Kendall A. Elsom, M.D., Stanley Schor, Ph.D.,
Thomas W. Clark, M.D., Katharine O. Elsom, M.D.
and
John P. Hubbard, M.D., Philadelphia

Records of medical examinations of 1,513 persons in executive positions were studied to estimate the value of periodic health examinations and to determine which phases of such examinations would be most productive of the desired results. At the first examination 612 persons (40%) were found to have previously unrecognized disease, 473 (31%) were free from new disease but had previously recognized impairments of health, and 428 (28%) were classified as healthy. Reexaminations were carried out in 822 persons after an average lapse of 16 months and yielded 386 new diagnoses. In about half of the cases of newly detected disease, the disease was capable of causing death or major disability, and in about 93% the condition was amenable to therapy. The data demonstrated the value of such examinations to the patient and established the relative frequency of the diseases to be watched for.

The periodic health examination is now widely practiced and even more widely recommended. The medical literature contains many reports of the yield of this procedure in terms of amounts of disease discovered. Available information, however, leaves much to be learned about the practical usefulness of the procedure, mainly because we do not, in general, know what would have happened without it. Thus, how frequently does the periodic health examination uncover significant disease which will, if unchecked, seriously affect the later health of a person? Is the disease so discovered amenable to treatment? Is time of importance in the application of therapeutic measures so that the detection of disease early rather than late makes a difference to the well-being of that person and to his life expectancy? These are basic questions which must be answered in the evaluation of the periodic health examination.

In addition, certain practical questions arise. For example, what are the most productive parts of the examination? Can a greater amount of disease be detected more economically by different procedures or new techniques? Can an adequate health examination be made available to people at a price they can afford? Many more such questions come readily to mind.

As the first step in a long-range investigation of the value of the periodic health examination, we have undertaken a retrospective analysis of the nature, distribution, and amenability to treatment of disease detected among 1,513 persons examined at the University of Pennsylvania Diagnostic Clinic from 1949 to 1958.

Material and Methods

Population.—All persons comprising the population studied are in management and in executive-level positions. They are employed in industrial plants both large and small, in banks, in a large chain of food supermarkets, in law firms, and in other enterprises. A total of 64 companies and organizations participated in the program during this period; most are in and around Philadelphia, many 50 to 75 miles distant, and one is [illegible] the middle South.

The periodic health examination was offered to these persons by their companies on a voluntar basis, the cost being borne by the organizat which they are employed. Of all of those to whom this service was offered, 96% accepted it. The number from any one organization varied from 3 to 300. The population was predominantly male and included only 13 females. The average age was 45 years, with a range from 24 to 76 years.

Of the 1,513 persons, 822 were examined at the clinic on two or more occasions, the average time interval between the first and second visit being 16 months; 83% of the intervals lay between 6 and months.

Examination.—The examinations inclu Every
tailed medical history and physical aris and re-
an internist. Forty-eight diffe tant prophylactic
few exceptions Board-cer developed a staphylococ-
inations. Investigat y 25% of the pemphigus vul-
hemoglobin est o received steroids alone were
cell count ected. Again, it appears likely that the
te ylactic administration of antibiotics had an
influence in increasing the incidence of staphylococcic infections in patients with pemphigus vulgaris.

From the University of Pennsylvania Diagno
partment of Preventive Medicine, School of

sultations were included when the examining physician considered them advisable for diagnostic purposes. About two-thirds of the persons examined had one or more additional procedures or consultations. Diagnoses were made by the examining physicians on completion of all of the studies carried out on each person. Each physician was free to make diagnoses according to his clinical judgment.

Table 1.—*Ten Most Frequent Diagnostic Categories Among 1,513 Executives, with Grading and Frequency of Occurrence*

Diagnosis: Class and Grade* A	B	C	Disease	No. of Times Diagnosed† 1st Examination	2nd Examination	Total
3	1	2	Obesity	137	45	182
2	3	2	Hypertension	124	33	157
			Anorectal lesions	94	37	131
4	3	4	Cryptitis	1	0	1
4	3	4	Fissure	4	0	4
4	3	4	Granuloma	1	0	1
3	1	4	Hemorrhoids	76	33	109
4	3	4	Papillitis	3	1	4
4	3	4	Papillae, hypertrophied	8	1	9
4	3	4	Proctitis	1	2	3
			Colonic polyps	87	25	112
1	1	2	Benign	84	25	109
1	1	1	Malignant	3	0	3
			Prostatic lesions	47	20	67
2	1	3	Benign hypertrophy	37	14	51
1	1	1	Carcinoma	1	2	3
1	1	2	Nodule	1	0	1
3	2	3	Prostatitis	8	4	12
2	1	2	Inguinal hernia	35	5	40
1	3	2	Diabetes	28	7	35
3	3	3	Anxiety state, mild	16	9	25
			Arteriosclerotic heart disease	14	4	18
1	3	2	Angina pectoris	4	1	5
1	3	2	Arteriosclerotic heart disease (unspecified)	6	1	7
1	3	2	Coronary heart disease	2	1	3
1	2	1	Myocardial infarction	2	1	3
2	2	2	*Peptic ulcer*	11	10	21
				593	195	788
			Total, all Diagnoses............	906	389	1,295

* Class A, potential seriousness of disease. Results if not treated: grade 1, deaths; grade 2, major disability; grade 3, minor disability; and grade 4, insignificant disability. Class B, optimal effect of known treatment, likely to result in improvement of: grade 1, eradicated; grade 2, arrested; grade 3, ameliorated; and grade 4, outcome not affected. Class C, urgency of treatment required: grade 1, urgent within days; grade 2, not urgent but promptness still indicated; grade 3, early therapy helpful though not presently required; and grade 4, time not important in terms of inauguration of therapy or progress of disease on basis of knowledge of disease.

† Figures to the right in columns "1st Examination," "2nd Examination," and "Total" indicate number of times a diagnosis listed under a general heading occurred.

Classification of Diagnoses.—Each diagnosis was
th[illegible] independently and separately by three of
[illegible] W. C., and K. O. E.) according to
[illegible]; class A, the potential serious-
A 24-year-old ma[illegible] B, the optimal effect of
the morning of July [illegible] urgency of action re-
hoarseness and a sore throat. It [illegible] arrived at only
tion. Examination revealed the patie[illegible] Each of these
ately hoarse and to have an injected pha[illegible] of
out exudate or local adenopathy. His tempera[illegible]
was 97.6 F (36.4 C). Indirect laryngoscopy was not

every instance. However, the 10 *most frequently* occurring diagnostic categories comprising 23 clinical entities are listed in table 1. These account for over 50% of all diagnoses made on first and second examinations and suffice to indicate the manner in which we have evaluated the seriousness, urgency, and amenability to treatment of the diseases occurring in the population under study.

This method of classification provides no information as to the severity or stage of development of the disease existing in a given person at the time of examination, but deals only with the nature of the disease itself and its potential seriousness. Similarly, in evaluating the amenability to treatment, no judgment was made as to whether, in a particular instance, treatment would likely be successful or unsuccessful. We have attempted only to determine whether or not effective treatment is available for the diseases encountered. A separate report will deal with some of these diseases in terms of the stage of development, severity, rate of progression, and the results of treatment in the individual patient.

Since our use of the term "disease" to describe certain deviations from normal might convey a misleading impression, brief comment on that point seems advisable. We do not imply, for example, that a person who is slightly overweight is necessarily ill, that a rectal polyp constitutes a serious threat in every instance, or that a mild elevation of blood

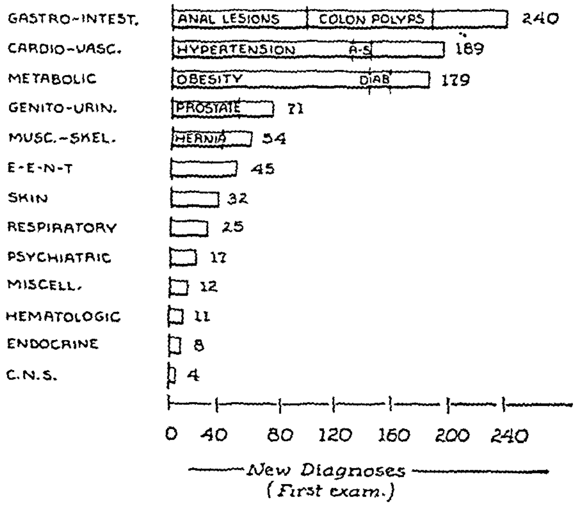

Fig. 1.—Distribution of disease by body system in 612 persons having newly detected disease on first examination.

pressure renders a person unhealthy. Perhaps another term for such conditions would be preferable but, since the ultimate effects of these deviations from normal are unknown in the individual instance and may produce significant illness, we have elected [illegible] the term "disease" with the qualifications

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Dr. Hesch is now at the University of Washington Hospital, Seattle.

Results

Frequency of Newly Discovered Disease.—Of the 1,513 persons receiving an initial examination, 612 (40%) were found to have previously unrecognized disease. Of the remaining 901 persons, 428 (28%) were diagnosed as "healthy," that is, were free from new disease and had no previously recognized disease which adversely affected their present health, while 473 (31%) were free from new disease, but had had illness which currently had an adverse effect on their physical status so that they could not be considered entirely "healthy."

On first examination, 906 new diagnoses were made in the 612 persons having new diseases and these diagnoses were distributed among the various body systems as indicated in figure 1. Diagnoses of disease involving the gastrointestinal tract (240), the cardiovascular system (189), the metabolism (179), the genitourinary tract (71), and the musculoskeletal system (54), constituted 81% of the total.

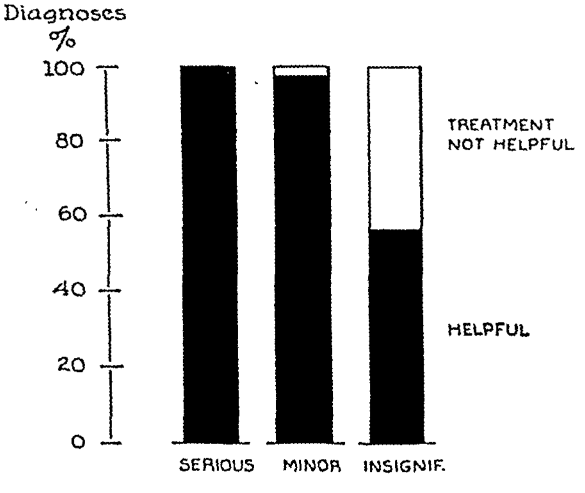

Fig. 2.—Percentage of new diagnoses made on first examination by optimal result of treatment and seriousness of disease.

Importance of Newly Discovered Disease.—Disease, according to the classification described above, was believed capable of resulting, if unchecked, in death or major disability in over one-half (57%) of the 612 persons in whom new disease was diagnosed on the initial examination. In one-third (34%) it was judged capable of producing minor disability, while in the remaining 9% the disease was judged insignificant. Expressed in terms of the total population of 1,513, 23% had disease of serious potential (i. e., grades 1 and 2 of cl[illegible] as shown in table 1), 14% had minor dis[illegible], and 4% had insignificant disease. The re[illegible]der, as previously noted, had no newly d[illegible]covered disease. If one calculates the proportion of the total number (906) of newly discovered diseases according to seriousness, 46% (416) were classified as serious, 40% (361) as minor, and 14% (129) as insignificant.

For most of the disease conditions detected (93%) therapeutic measures are available which are considered beneficial (fig. 2). (In figure 2 and 3, "treatment helpful" includes grades 1-3 of class B, as shown in table 1, and "treatment not helpful" includes grade 4 of class B). These beneficial therapeutic measures can eradicate the disease, as, for example, the excision of a cancer; they can arrest disease, as in pulmonary tuberculosis; or they can ameliorate disease, as in peptic ulcer. We have not tried to judge whether in each person treatment will be beneficial, but merely whether known measures exist which can influence the disease or condition favorably. For instance, obesity may or may not be looked on as a disease, may or may not require treatment, and, in a given individual, may or may not respond to measures instituted to correct it, but in terms of our classification obesity is a condition for which, under optimal conditions, successful therapy exists.

TABLE 2.—*Distribution of New Diagnoses of Disease on First Examination of 612 Executives*

Persons, %	Diagnoses Made, %
0.4	3.3
1.3	9.5
3.9	22.5
13.2	53.9
40.4	100.0

From the point of view of the urgency with which treatment was indicated, only a small proportion (2%) of the new conditions required urgent action within the ensuing few days. (The diseases detected which fall into this category were few, namely: congestive heart failure, in one person when he returned for his second examination; malignant hypertension, developing in one person be-

TABLE 3.—*Expected and Observed Distribution of New Diagnoses of Disease on First Examination of 1,513 Executives**

Diagnoses, No.	Observed in Persons, No.	Expected in Persons, No.†
0	901	835.0
1	411	496.1
2	141	147.4
3	40	29.2
4	14	4.7
5	6	[illegible]
	1,513	[illegible]

* Probability of $\chi^2 \geq$ observed is less than 0.001

† If diagnoses were distributed by chance [illegible] curve which gives the probability of occur[illegible] continuum of time.

ecafat in n. A consecu- evaluated as to their of the abnormalities or

tween examinations [illegible]ed in them by the examina- on initial exa[illegible] malignancy was unknown, as were with [illegible] all of the gynecologic disease and lab- inatory abnormalities, as well as 72% of the diastolic and 63% of the systolic hypertension (fig. 3). Unknown medical and surgical disease processes involving other body systems ranged between 6%

tion in a colonic polyp, in three persons on initial examination; kidney stone, in one; kidney abscess, in one; ureteral calculus, in two; carcinoma of the prostate, in two; ruptured tendon, in one; and tuberculosis in one person.) However, more than one-half (57%) were believed to require prompt therapeutic action if the course of the disease was to be influenced effectively. For 21% no immediate therapeutic action was required, but knowledge of the presence of the disease was considered helpful since therapy might be required ultimately. Finally, in 20% time was not considered important either in the inauguration of therapy or in the progress of the disease.

Distribution of Newly Discovered Disease.—Much of the disease detected was concentrated in a small proportion of those examined. Thus, while all of the newly discovered disease was found in 40% of the population, more than one-half of this disease (54%) was concentrated in only 13% of the group (table 2). Statistical analysis suggests that some factor or factors other than chance (table 3) were operating to bring about concentration of disease in this small segment of the group. This phenomenon was apparent, even holding age constant, for all disease, serious or trivial, old or new, and whether detected on the first or on the second examination. Those persons having multiple serious diseases also ad multiple minor or insignificant diseases, and as ay as seven different body systems were involved [illegible] same person. These multiple diseases usually the [illegible] be unrelated to each other. In persons ing into the mo[illegible] more diagnoses were made at a such as stress reaction [illegible] approximately one-fourth education in periodic health [illegible]med to have an etiologi- bination of factors which becam each other. Some particular stage of the natural course [illegible]ble 4.

The types of clinical findings were co[illegible] of bias throughout the 12-year period to the degree that the various types of abnormalities may be anticipated on a percentage basis of the total number of examinees. This is particularly significant in view include all abnormalities another might record only the primary diagnosis. We have, in fact, observed some physician difference in this regard. However, it would be reasonable to expect that both such examiners would record all serious diseases while the former would also record a number of clinically unimportant conditions. Thus, multiple diagnoses due to physician difference would tend to include an excess of minor conditions. Our results, on the contrary, indicate that the phenomenon of concentration of disease in a small segment of the population applies to both major as well as minor conditions and probably cannot be explained by difference between physicians.

Relationship of Age to Seriousness of Disease and Amenability to Treatment.—The number of new diagnoses was found to increase in direct proportion to age (fig. 3). This rise reflected a much greater increase in disease of potential seriousness than in minor or insignificant disease. The proportion of disease judged amenable to treatment, however, was the same in all age groups. Of the total of all the newly diagnosed disease more than 60% was potentially serious in the older age group, compared with slightly over 30% in the youngest group (fig. 4).

Relationship of Time of Examination to Frequency and Type of Newly Discovered Disease.—As noted above, 822 members of the group were examined a second time by June 30, 1958.(Although this study covers the period 1949-1958, a large number of persons entered the periodic health examination program in 1958 and had not yet returned for their second examination by the time analyses were begun.) When the number of diagnoses of new disease made on first and on second examination was compared in these persons, very little difference was observed in the rate of occurrence of disease per unit of population. Thus, on the first examination, the amount of newly detected serious disease was 56 new diagnoses per 100 subjects [illegible]ined, and on the second examination 47 new

Quest[illegible]

(Dec.) 1954

TABLE 4.—*Clinical Conditions, Body Systems, and Possible Relationship of Diseases in Three Persons with Multiple Diagnoses*

Case No.	Diagnoses Known on Admission*	New Diagnoses, 1st Examination	New Diagnoses, 2nd Examination	Diagnoses, No.	Body Systems Involved, No.	Possibly Related Conditions in Each Person, No.
937	Duodenal ulcer Varicosities, bilateral Xanthelasma Dermatophytosis Fibrotic epididymitis	Hypertension	Rectal polyp	7	4	0
884	Tuberculosis, old, inactive Psoriasis Chronic low back pain	External hemorrhoids Benign prostatic hypertrophy Hypercholesteremia† Elevated postprandial sugar level†	Diabetes mellitus† Deafness, unknown cause	9	7	3
68	Essential hypertension†	Diabetes mellitus† Benign prostatic hypertrophy Diverticulosis of colon Rectal polyp	Cholelithiasis†	6	4	3

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*Conditions, recognized on admission, but already known to the person, are here included in order to obtain as complete a clinical picture as possible of each subject.

†Specific diseases, possibly related to each other.

diagnoses per 100 subjects examined. A slight increase in disease of minor disability-potential was found on second examination, while the amount of insignificant disease was negligible in each examination.

As the time interval between examinations increased from one to two years or more, a steady though small increase in the number of diagnoses per unit of population was noted on the second examination (table 5). The smallness of the increase or even the increase itself could have been brought about by advancing age, since the number of diagnoses also increases with age. However, when the data were examined by age group, a slightly greater increase in the number of diagnoses was observed for those of similar age than for all persons, as the interval lengthened. This is shown in table 5 for the age group 40 to 49.

Comment

The finding of disease in 40% of the executives we examined agrees well with results from other clinics.[1] In general we have found that a high proportion of the disease discovered was potentially threatening to the person involved. Furthermore, effective treatment is available for most of the conditions encountered. The extent to which the early discovery of these potentially serious diseases has had a significant effect on the progress of the disease or on the health and productivity of the person involved is still undetermined. We are at present attempting to gain information on these questions by studying what has happened over the years to those persons in whom disease was detected in an early stage.

TABLE 5.—*Number of New Diagnoses Made Per 100 Executives Examined on Second Examination by Interval Between First and Second Examinations*

Interval, Yr.	All Ages, No.	40-49 Yr No.
Under 1	45	42
1 to 2	47	45
2 and over	51	55

The high prevalence of potentially serious disease in members of the "executive" category who are of favorable socioeconomic and educational status makes it reasonable to expect an even higher prevalence of serious latent disease in the population at large. This is indicated by the study made by the Commission on Chronic Illness[2] of a cross section of the population of Baltimore. Here the over-all frequency of chronic disease was found to be 1.6 conditions per person, a figure closely approximating 1.4 conditions per person in our population, if all chronic diseases, both newly discovered on first examination and previously known, are taken together.

Increase in the amount of disease with advancing age is a well-known phenomenon. That this increassessing as observed in our population, was due primal potentials

disease of serious potential and that such disease, if promptly and properly treated, may be favorably influenced indicates the need for close cooperation between the diagnostic clinic physicians and those

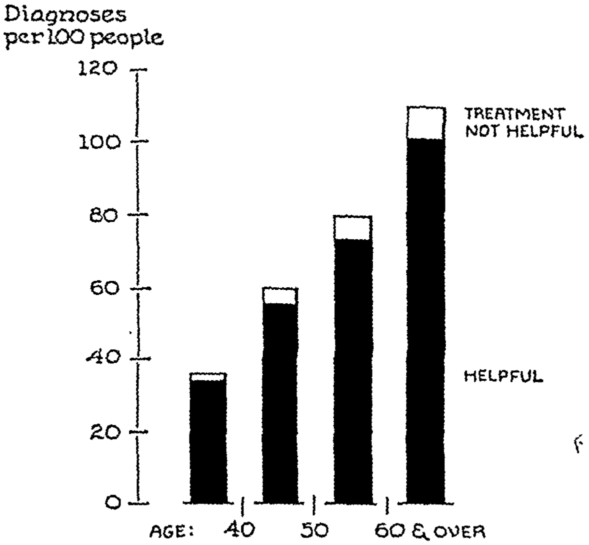

Fig. 3.—Number of new diagnoses made per 100 persons examined for first time by age and optimal result of treatment.

responsible for therapy. It is in the hands of the practicing physician that the effectiveness of this aspect of preventive medicine untimately rests.

The concentration of 54% of the total amount of detected disease among 13% of those examined, and the presence within this group of a disproportionate

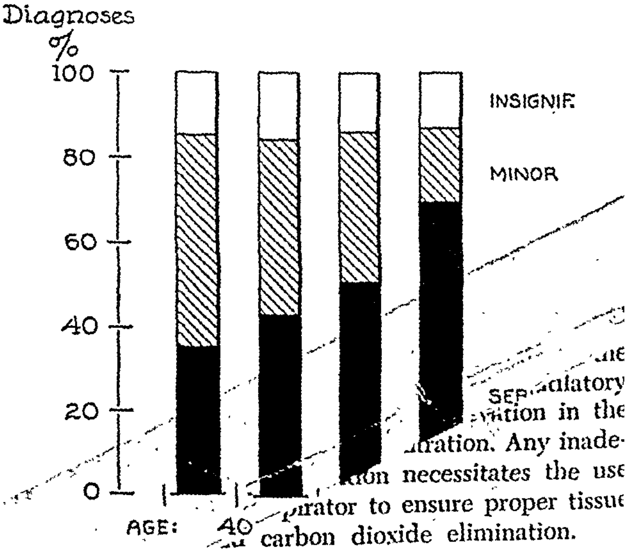

Fig. 4.—Percent

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cular manifestations of severe systemic tetanus is accomplished by adequate suppression of reflex muscle spasm without serious impairment of res- piration or consciousness. The clinical use of the ad- vocated sedative-relaxant regimen approaches this

Densen and co-workers[3] have observed that in the Health Insurance Plan of Greater New York 50% of the medical services are utilized by only 12% of subscribers. Hinkle and Wolff[4] found, in a study of three different population groups, that a small proportion of the persons studied suffered a greater number of illnesses of all types than did others. It is interesting to note that even in the population studied by us, which consisted of subjects who did not generally recognize illness in themselves and who, consequently, did not report to us for the purpose of medical treatment, evidence of disease was similarly confined to a relatively small segment of the group.

Summary and Conclusions

Findings of a retrospective study of the periodic health examination records of 1,513 executives were as follows: 1. In 612 (40%) new diagnoses were made. The number of diagnoses made on the same persons on second examination was only slightly less than on the first. 2. Of the newly detected disease, 46% had the potential, if unchecked, of producing death or major disability. In the total population studied, 23% of the subjects were found to have disease of this type. 3. For almost all of the diseases detected (93% in our judgment) therapy is available which, if applied at the proper time, can be expected in some instances to remove the disease, in others to arrest its further development, or, at the least, to ameliorate the condition. 4. Of the disease diagnosed on first examination, 54% was concentrated in 13% of the population, more than would be expected by chance. 5. The amount of disease increased steadily with age, diseases of serious potential increasing by a much larger proportion than the less important conditions. 6. Prompt therapy was considered indicated in more than one-half of the diseases detected.

3600 Spruce St. (4) (Dr. Elsom).

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Dr. J. Corbett McDonald, the Central Public Laboratory, London, England, made many contributions to this study.

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SYMPTOMLESS RESERVOIRS OF RABIES VIRUS.—Studies on the pathogenesis of rabies in two species of experimentally infected insectivorous Chiroptera, the Mexican free-tailed bat *(Tadarida mexicana)*, a quasi hibernator, and the little brown bat *(Myotis lucifugus)*, a deep hibernator, provided evidence that brown adipose tissue may serve as an extraneural site for storage and multiplication of rabies virus. Although the Mexican free-tailed bat proved to be relatively insusceptible to experimental rabies infection, virus was demonstrated in the brown fat of 22 per cent of those animals shown to be infected by viral assay in white Swiss mice. Rabies infection in this species was most evident 20 to 40 days after intramuscular inoculation of virus. Rabies virus was found to be widely distributed in the little brown myotis 9 to 26 days following inoculation, and virus concentrations in some of the tissues approached the level of the stock mouse brain virus suspension used in inoculating these bats. . . . In the experimentally infected *Myotis lucifugus* and in the Syrian hamster which is highly susceptible to infection, rabies virus was isolated more frequently from the brown fat than alivary gland *indicating that in a susceptible host brown adipose tissue* ent a site of viral proliferation as salivary gland. Since rabies virus for long periods of time in the brown fat of experimentally sionally demonstrated in this tissue alone, it is suggested a mechanism by which these animals may serve

—S. E. Sulkin, Ph.D., P. H. Krutzsch, Ph.D.,
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The patient with tetanus may conti
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by the use of a gently inflated rubber cuff which
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In addition, the insertion of a gastric tube may be

PROPHYLACTIC ADMINISTRATION OF ANTIBIOTICS IN PATIENTS RECEIVING STEROIDS SYSTEMICALLY

Richard Carl Gibbs, M.D., Laszlo Biro, M.D.
and
Marion B. Sulzberger, M.D., New York

We[1] studied the influence of prophylactic, concomitantly given doses of antibiotics on the incidence of staphylococcic infection in patients treated with steroids on the dermatological wards of Bellevue Hospital. True, steroid therapy alone is not without hazard in this respect,[2] but, as will be seen from our study, the prophylactic addition of antibiotics certainly does not always succeed in preventing infection and may, in some cases, convert a potential hazard into reality.

Subjects and Procedures

We studied all admissions to the dermatological service of Bellevue Hospital over a nine-month interval (July 1, 1958, through March 31, 1959). From all admissions, we divided the patients into the following treatment groups: (1) patients receiving neither steroids nor antibiotics, (2) patients receiving antibiotics only for specific infectious processes, (3) patients receiving steroids only, (4) patients receiving steroids and concomitant prophylactic doses of antibiotics, and (5) all patients admitted (groups 1-4).

The table shows the incidence of staphylococcic infection by treatment groups and points to one obvious and striking fact: patients in group 4, i. e., those given both steroids and prophylactic doses of antibiotics, had the highest incidence of staphylococcic infection.

Comment

The question arises as to whether the patients in group 4 differed from those in the other groups, not only in the matter of receiving both steroids and prophylactic doses of antibiotics but also in other ways which may have increased their susceptibility to staphylococcic infection. Or was it the addition of prophylactic doses of antibiotics which, in reality, gave rise to this increase?

To answer these questions, we investigated group 4 from several points of view. Thus, age, sex, diagnosis, and length of hospitalization of the patients in this group were compared to similar characteristics of the patients in the other groups in an attempt to determine their differences or similarities. In addition, incidence of infection in all groups was calculated and compared according to diagnosis and age.

On the average, the patients included in group 4 were somewhat older than the patients in the other groups, but they were not remarkably older than the average age for all groups. Moreover, if the incidence of infections is calculated for each age group, it is found that the patients in group 4 tended to have an above-average incidence of infection. It was noted, however, that the highest over-all incidence of infection occurred in one of the older age ranges (71-80 years). It appears, therefore, that the prophylactic administration of antibiotics together with steroid therapy may increase the incidence of infection in most age ranges. However, older patients were more likely to get infections, regardless of their forms of treatment. Our figures did not indicate that sex was a significant factor in determining staphylococcic infection.

Incidence of Staphylococcic Infection by Treatment Groups

Treatment Group		Infection	
Drug Given	Patients, No.	No.	%
Neither steroids nor antibiotics	192	5	2.6
Antibiotics only	41	3	7.3
Steroids only	42	5	11.9
Steroids and concomitant prophylactic doses of antibiotics	31	14	45.1
Total no. of patients admitted (groups 1-4)	306	27	8.8

Although the diseases of the patients in group 4 tended to be more serious and debilitating than those of the patients in the other groups, the calculation of incidence by diagnoses for all five groups made it apparent that again the patients in group 4 were more likely to develop staphylococcic infection. In fact, in about one-half of the skin diseases included in our study, the percentage of staphylococcic infections occurring in patients with that disease in group 4 was higher than the percentage of
staphylococcic infections in the total numb[illegible] al
patients with that particular skin dis[illegible] may be
patient who had pemphigus [illegible] by mechanical
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pro[illegible]tanus depends on the amount of toxin that combines with the central nervous system. The duration of the incubation period provides a rough index as

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[1] From the Department of Dermatology and Syphilology of New York University Post-Graduate Medical School and the Service of Dermatology and Syphilology of Bellevue Hospital. Dr. Biro is a Charles R. Rein Fellow in Dermatology.

Patients in group 4 had, on the whole, a longer hospitalization than the patients in all other groups, except group 3. Would this explain the increased incidence of infection? Probably not, because, if the average length of hospitalization before staphylococcic infection developed is calculated for the patients in group 4 who developed infection, the value (4.9 weeks) is less than the average length of hospitalization for all groups of patients (5.3 weeks).

One other facet of the problem was investigated. We tried to ascertain if the percentage of patients receiving steroids and prophylactic doses of antibiotics happened to be greatest at a time when staphylococcic infections also happened to be most frequent on our wards. This did not appear to be the case. As a matter of fact, the chronological distribution of the 27 patients who developed infection was even throughout the study period, except for a slightly increased frequency in the months of August and September. However, in August and September, the percentage of patients receiving steroids and concomitant prophylactic doses of antibiotics was actually slightly decreased.

Monilia infection of the mouth was a complication in four of our patients who developed staphylococcic infection. All of these patients were receiving antibiotics at the time of infection.

Summary

The results of our study indicate that prophylactic treatment with antibiotics of patients receiving steroids did not decrease and, indeed, may have contributed to an increased incidence of staphylococcic infection in these patients.

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ANAPHYLACTIC DEATH FROM USE OF A THROAT LOZENGE

Capt. Donald J. Hesch (MC) U. S. Army (Res.)

A 24-year-old man complained of hoarseness and sore throat of 10 to 12 hours' duration. When examined he showed signs of laryngitis and pharyngitis but was free from fever and signs of respiratory obstruction. Circumstantial evidence later showed that immediately after the examination he took a lozenge containing 10 mg. of benzocaine, 1 mg. of tyrothricin, and chlorophyll. Acute and increasing respiratory distress appeared promptly, and he was pronounced dead some 20 minutes after he had reported for the examination. Analysis of the postmortem findings and other data indicated that the fatality was due to anaphylaxis.

In office practice lozenges have found wide use for the relief of acute sore throats. The usual active ingredient of these preparations is a local anesthetic, an antibiotic for local use, or a combination of the two. With the increasing number of drugs in each of these classes, there has been a similar rise in the consumption of troches. Each has its own particular combination of drugs and dosage. Unfortunately, with the expanding use of any drug the incidence of untoward reactions also rises. The purpose of this report is to present a fatality presumed to be due to anaphylactic shock resulting
am such a lozenge and to offer comments on
severe ally safe medicaments.
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Report of a Case

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done. No respiratory impairment was noted. On the basis of these findings and the types of sore throats seen recently at the same installation, a diagnosis of acute viral pharyngitis and laryngitis was made. The patient was treated with a standard throat lozenge, containing 10 mg. of benzocaine, 1 mg. of tyrothricin, and chlorophyll. In addition, he was given an alkaline gargle and voice-rest instructions.

After receiving the medicaments he departed for his barracks, two blocks distant. As he approached his living quarters he was noted to stagger and required the assistance of his barracks mates to reach a bed. Pinkish froth was described issuing from his mouth and nose at this time. There was acute and increasing respiratory distress, and a gurgling was noted in his throat. He became comatose and died before adequate first aid could be begun. He was pronounced dead by a medical officer some 20 minutes after he was first seen at the dispensary.

At autopsy the mouth contained no foreign material and was free of open lesions. The larynx exhibited marked edema of the cords, particularly of the aryepiglottic folds and glottic chink. There was complete obstruction of the airway at this level. In each side of the margin of the epiglottis was an oval cystic structure, measuring 10 mm. in diameter, filled with a large quantity of thick, greasy, yellow, grumous material. The larynx and entire tracheobronchial tree down to the small bronchi was filled with copious amounts of frothy, pink fluid. The lungs were voluminous, hypercrepitant, and bulged from the thoracic cavity when the chest plate was removed. Tiny air-filled blebs were noted beneath the pleural surface of all lobes. The cut surfaces of the lungs exuded large quantities of the same frothy, pale pink fluid. The remainder of the gross findings were normal for a 24-year-old male.

Microscopic examination of the lungs demonstrated extensive areas of congestion and edema alternating with areas of hyperdistended alveoli. The bronchi were filled with collections of serum, red blood cells, and leukocytes. The larynx, superior to the vocal cords and extending to the base of the epiglottis, showed extensive edema, principally of the submucosal tissues, extending to the muscular coat and interstitial connective tissue. The epiglottis was also edematous. The nodules noted grossly were found to be small abscesses bounded by granulation tissue. No micro-organisms could be identified. The remainder of the microscopic examination showed only marked vascular congestion of all visceral organs.

Blood culture revealed an organism of a Pseudomonas species, felt to be a postmortem contaminant. Toxicological examination of samples of brain, liver, kidney, and lung was unrewarding.

Cause of Death.—The chain of events leading up to this man's acute respiratory death is, in part, arrived at through deduction from known facts. On investigation, the number of lozenges found on the body was one less than that prescribed. The pharmacist maintains that his count was accurate. Apparently, the man had placed one of these in his mouth on receipt of the medicament, which might be assumed for one in distress from a sore throat. The time required to walk back to his quarters was certainly no more than 10 minutes, and within this time his symptoms began. Therefore, there must have been some acute change in the patient's environment rather than a coincidental and catastrophic exacerbation of existing epiglottic disease. I believe that this acute change resulted from the consumption of the lozenge and an idiosyncracy to either benzocaine or tyrothricin. There is no evidence from his health records that he received any unauthorized penicillin therapy at this time nor that he had any history of allergy.

Toxicity of Local Anesthetics

Systemic toxicity of a drug depends on the amount in the circulation at any one time, which in turn depends on several factors. The first factor is the amount of drug administered, its potency, and concentration. Rate of absorption from site of application or injection must be considered, as well as the rate of destruction and elimination, inadvertent vascular injection, solubility of the material, and its ability to diffuse through mucous membranes. The last and, in this patient, most important factor is patient susceptibility.

Reactions to local anesthetics can occur irrespective of the route of administration. They are most common after topical application. Adriani and Campbell[1] discount the hypothesis that there is a change as the anesthetic passes through the mucous membrane or skin, rendering it more toxic. Recent evidence indicates that most toxic reactions from local anesthetics are associated with high plasma drug levels due to rapid absorption. Topical application of a given dose results in blood levels which closely simulate those obtained after rapid intravenous injection.[2] Absorption from mucous membrane is second only to that from an intravenous injection, and after an equivalent dose has been applied to the pyriform fossa, a peak one-third to one-half as great develops in four to six minutes. These drug levels are a function of the total dose and not of the concentration.

Reactions to local anesthetic drugs may be divided into toxic and allergic types. Those listed as toxic are the circulatory or depressant type and the stimulating or convulsive type. Allergic reactions may be classed as contact dermatitis, serum sickness patterns, atopic reactions, and anaphylactic shock. It has been stated that 99% of all reactions to local anesthetic agents are not allergic or anaphylactic unless accompanied by a skin reaction.[3] Thus, overdosage rather than hypersensitivity leads by far as the cause of reactions to local anesthetics. The suddenness with which the shock may occur, however, does not always permit the development of skin eruptions, asthma, or signs usually associated with drug sensitivity. A rare histamine-like reaction which Criep and Ribeiro [4] reported in three severe allergic reactions is characterized by only hypersecretion of the lungs and bronchospasm.

Benzocaine Toxicity.—Fatal reactions to local anesthetics are not new, and deaths have been reported [5] as due to cocaine, procaine, and tetracaine. Death from benzocaine apparently has not been reported. It is one of a group of esters of aminobenzoic acid, ethyl aminobenzoate, related to the procaine group. This common basic structure of several of the local anesthetics has been responsible for cross-reactions not only among themselves but with other drugs. It is suspected to be responsible for reactions on the first application of a local anesthetic to persons who may have acquired sensitization from nontherapeutic agents with the same basic configuration, e. g., the azo dyes of colored food stuffs.[6]

Benzocaine lacks the tertiary amino group and thus does not form soluble salts. In this last fact lies the general belief of its relative safety. Recent studies by Campbell and Adriani [2] have now shown that the free base of a local anesthetic is almost as rapidly absorbed from mucous membrane as the salt. Reactions to benzocaine do occur and several cases of nonfatal methemoglobinemia have been reported [7] from its use. Gaul [8] has reported a case of severe dermatitis after benzocaine application in a person previously proved sensitive to paraaminobenzoic acid in sunburn lotion.

Tyrothricin Toxicity.—In contrast, tyrothricin is a highly active poison. It contains two components, gramicidin and tyrocidine, and its toxic effects are the sum of the actions of these. It is a very active hemolytic agent, causing damage to the spleen, kidneys, and liver. Meningeal and cranial nerve damage has occurred from its use in sinus irrigation. Injection of small amounts causes death within a relatively short time. Therefore, its use is restricted to local application, and it is not used on fresh wounds or for sinus irrigation. When used orally it is of low toxicity; it is used in troches for its bactericidal properties with safety. It is not absorbed from the gastrointestinal tract and is inactivated by blood, peptone, and other body fluids.

When properly used by local application, it makes few if any undesirable side-reactions. Hypersensitivity reactions are practically unknown, the most severe to be reported [9] being a case of contact dermatitis due to tyrothricin in a person sensitive also to other antibiotics. Fifty-one nurses were tested by patch technique with various antibiotic agents, and two reacted to tyrothricin.[8] Bleeding has occurred after the use of alcoholic solutions of the drug applied to fresh wounds.[10]

Postmortem Findings After Fatal Reactions.—The postmortem findings in reports of fatalities resulting from local anesthetic drugs indicate capillary congestion, alveolar transudation, areas of emphysema and atelectasis, hemorrhagic foci in various organs, visceral congestion, and dilatation of the right side of the heart. Animals dying after lethal doses of tyrothricin show nonspecific changes of acute congestion of the lungs and abdominal viscera, petechial hemorrhages of the spleen, kidney, and myocardium, and fatty degeneration of the liver with necrosis, cloudy swelling of the tubular epithelium of the kidney, and glomerular hemorrhage.

Comment

There are 19 throat lozenges on the market, manufactured by major drug firms, which contain either benzocaine or tyrothricin [11]; 10 of this number contain both. The usual dosage is 3 to 10 mg. of benzocaine and 1 to 3 mg. of tyrothricin. These figures do not include many other such preparations available in the local drugstore. Many and possibly all can be obtained without a prescription. Therefore, it is suggested that at some previous time this person had used a like preparation and had become sensitive to benzocaine or tyrothricin. It is possible, too, that he had become sensitized through use of a nontherapeutic agent. The low doses involved and the anaphylactic nature of the clinical course point to a sensitivity reaction, rather than overdosage toxicity, with the rapid absorption through the pharyngeal mucous membrane triggering the reaction. I believe the epiglottic abcesses to be only a contributing factor and not the basic cause of death.

After reviewing the literature, I believe this to be the first reported case of its kind. The fact that anaphylaxis can occur from local application of a drug should indicate the need for more respect for topically given drugs prone to evoke sensitivity reactions. It is disturbing to consider the amount of such drugs used annually in troches alone, particularly since they are so easily obtained.

Summary

A case of rapid death has been attributed to a topically used medicament in a common throat lozenge. The relationship of administration of a lozenge, containing benzocaine and tyrothricin, to the sudden onset of symptoms points to a sensitivity reaction. The postmortem findings of obstructive emphysema and transudate extending to the small bronchioles indicate a systemic process rather than laryngeal spasm and edema alone. This is felt to represent human anaphylaxis. Increased respect should be given to the simple and commonly used medicaments so readily available to all.

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CONTROL OF NEUROMUSCULAR MANIFESTATIONS OF SEVERE SYSTEMIC TETANUS

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and
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Tetanus is a severe intoxication of the central nervous system characterized by generalized hypertonicity of the skeletal muscles and convulsive seizures. These manifestations result from the action of an exotoxin produced by *Clostridium tetani.*

The initial characteristic neuromuscular manifestation of severe systemic tetanus is stiffness of the jaw and neck muscles. The stiffness of the jaw muscles progresses to a tonic spasm producing trismus or lockjaw. The patient is apprehensive, hyperirritable, and restless. The eyebrows become raised, and the corners of the mouth twist in a spasm to form a sardonic grin. Difficulty in swallowing develops. Rigidity gradually extends to involve the trunk, with severe spasm of the posterior spinal muscles so that the back is arched in an opisthotonic position. The reflex spasm and convulsive seizures may be precipitated by the slightest stimulus, such as handling the patient or by visual and auditory stimulation. During the episode of severe muscle spasm, asphyxia may develop from closure of the glottis and compression of the thorax. The severity of the neuromuscular manifestations of

To arrest the progress of tetanus in a patient two main objectives must be attained, namely, the neutralization of circulating toxin and the elimination of its source. Meanwhile the neuromuscular manifestations must be controlled. Drugs used for this purpose are generally depressants of the central nervous system. If they hamper cardiovascular and respiratory function their use is illogical. The regimen advised by the authors employs a sedative (either secobarbital or pentobarbital) and a muscle relaxant (methocarbamol) together with chlorpromazine, which is believed to potentiate the sedative-relaxant effects of the other two drugs. Strict attention to pulmonary ventilation is essential. Tracheotomy should be performed early in severe cases. The aspiration of tracheobronchi[illegible] secretions must be prevented, and [illegible] necessary to assist respiration [illegible] means. In the preventi[illegible] anesthesiologist ca[illegible]

by [illegible] cians, with [illegible] made these exam- [illegible] routinely included were [illegible] on, white and differential blood [illegible] analysis, postprandial blood sugar de- [illegible] ion, serologic tests for syphilis, 12-lead electrocardiogram, and an anteroposterior roentgenogram of the chest. Sigmoidoscopic examination was performed on all persons aged 40 years or over and on younger persons when deemed necessary Additional laboratory procedures or clinical con

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to the subsequent intensity of the manifestations. The shorter the incubation period the more severe the neuromuscular manifestations.

In the *management of severe systemic tetanus,* early diagnosis is of vital importance so that treatment can be instituted promptly. After the diagnosis has been established, the primary aim is to halt the progression of the disease and to provide adequate supportive therapy during its self-limited course.

To arrest the progress of the disease, two main objectives must be attained. Of primary importance is the neutralization of any circulating toxin before it can combine with the central nervous system and produce further effects. This is accomplished by the intravenous and intramuscular administration of adequate doses of tetanus antitoxin. The second main objective is to eliminate the focus of infection to prevent the further production of toxin. In addition to surgical excision of the focus in which the clostridial organisms are living, multiplying, and producing toxin, antibiotic therapy should be used to prevent secondary infection.

A period of two to four weeks is required for the toxin to be released from the central nervous system and excreted from the body. Caloric intake, fluid and electrolyte balance, pulmonary ventilation, and suppression of the severe reflex muscle spasms must be maintained during this time.

Early Methods of Treatment

Therapeutically sound regimens for the administration of antitoxin have been formulated.[1] However, control of the neuromuscular manifestations *with the concomitant maintenance of adequate* alveolar ventilation has remained unsatisfactory. In the past, control of the neuromuscular manifestations of tetanus has been accomplished by the administration of massive doses of paraldehyde, chloral hydrate, bromides, barbiturates, opiates, and tribromoethanol (Avertin). The use of such massive doses of these central nervous system depressants is not only contrary to basic pharmacological principles but detrimental to the maintenance of normal cardiovascular and respiratory function. A balance
between central nervous system depression and
us ppression of muscle spasm is hard to achieve,
the follow ith use of the above drugs adequate control
ness of the dis muscle spasm is accomplished only by
treatment; and class tient to the hazards of respiratory
quired. The final designa epression. The added insult of
central nervous sys-
after agreement by *all* three assessors. ious effect of a
three classes was graded from 1 to 4 in t
probable consequences (table 1). ular
Since a total of 392 separate clinical entities were
encountered in our population, *it is not* practicable
to show in tabular form the gradings employed in

their inability to produce muscular relaxation without respiratory paralysis. There is a narrow margin of safety between the relaxing dose and the completely paralyzing dose.

New Methods of Treatment

Avoidance of Respiratory Impairment.—In 1910, Gilbert and Descomps[3] discovered that phenoxypropanediol produced reversible flaccid paralysis in animals. It was not until 1946 that interest in this property of the glycerol ethers was revived by Berger and Bradley.[4] Their studies of mephenesin (Tolserol) and related compounds stimulated the search for drugs capable of eliminating muscle tone without impairment of respiration or consciousness. Mephenesin, although an effective interneuronal depressant agent, is limited in its use, due to a transient duration of action, low water solubility, and significant hemolytic activity on intravenous injection of concentrations greater than 2%. In search for compounds that lack the disadvantages of mephenesin, many congeners have been synthesized and studied. The carbamate congeners were found to retain the muscle-relaxing action, to possess a longer duration of action, and to have greater water solubility.

Meprobamate (Miltown, Equanil) and methocarbamol (Robaxin) were found to have muscle-relaxant actions similar to those of mephenesin but of greater potency and longer duration. They both antagonize strychnine and pentylenetetrazol (Metrazol) convulsions. They decrease skeletal muscle tone without affecting the circulation, respiration, or autonomic functions. Meprobamate also has a sedative effect but has the disadvantage of causing thrombosis, hemolysis, and possible glomerular damage after intravenous administration. The complications which follow the intravenous administration of mephenesin and meprobamate have not been encountered with methocarbamol. The interneuronal depressant agents have a more specific and logical pharmacological action than the neuromuscular blocking agents to recommend their use in the control of the reflex muscle spasm of tetanus. These drugs act centrally at the internuncial pool of neurons by depressing the polysynaptic reflex arcs. The monosynaptic reflex arcs are unaffected. There is no direct influence on the motor nerve, skeletal muscle, or myoneural junction.

Mechanism of Interneuronal Depressants.—The synaptic organization and the pharmacological properties of synapses disclose the mechanism by which the interneuronal depressant agents exert their effect on the neuromuscular manifestations of such agents as tetanus toxin, pentylenetetrazol, and strychnine. It has been demonstrated that tetanus toxin and strychnine selectively affect the inter-
neurones of polysynaptic reflex arcs in the central
to vous system by suppressing inhibitory synaptic
stated. As a result, polysynaptic reflexes are ex-

aggerated and uncoordinated due to loss of inhibitory control. The clinical manifestations of this effect on the interneurones and the alteration in polysynaptic reflexes is a greatly exaggerated contraction of the flexor muscles and a simultaneous contraction, rather than relaxation, of the extensor muscles. Pentylenetetrazol affects the interneurones of polysynaptic reflex arcs by activating excitatory synaptic action. This explains the fact that pentylenetetrazol is capable of increasing reflex excitability after strychnine has been allowed to exert its maximal effect.

There is no known substance that primarily activates the inhibitory synapses. Thus it is postulated that methocarbamol and congeners selectively affect the interneurones of polysynaptic reflex arcs by suppressing excitatory synaptic action. Methocarbamol and congeners appear to possess the ideal pharmacological action to control the reflex muscle spasm characteristically induced by tetanus toxin as well as strychnine and pentylenetetrazol.

Sedative-Relaxant Regimen.—A sedative-relaxant regimen was formulated (fig. 1) which has proved to be effective in the control of the neuromuscular manifestations of severe systemic tetanus.[6] Methocarbamol was used to suppress reflex muscle spasm. This drug may be administered slowly intravenously, in large doses, as a saturated aqueous solution, with little danger of an appreciable degree of hemolysis as indicated by serum bilirubin and hemochromogen tests.[7] An initial single dose (about 15 mg. per kilogram of body weight) is administered intravenously until the desired suppression of reflex muscle spasm is achieved. A continuous intravenous drip infusion is then used to maintain muscle relaxation. Secobarbital (Seconal) or pentobarbital (Nembutal) (1 mg. per kilogram of body weight) is administered intravenously every four to six hours to produce psychic sedation and amnesia. In addition, chlorpromazine (Thorazine) (0.5 mg. per kilogram of body weight) is administered intravenously every eight hours to potentiate the sedative-relaxant effect. Chlorpromazine will abolish the muscle spasm of experimentally-induced tetanus in rabbits.[8] Large doses have been used also to control muscle spasm in cases of clinical tetanus. This drug probably acts by depression of the internuncial neurons as well as the hypothalamus and the reticular activating system.

Comment

The use of the intravenous route to administer drugs has two advantages. In addition to preventing excessive stimulation of the patient by multiple needle punctures, the intravenous route provides a more accurate means of assessing the dose-response relationship.

Dose-Response Relationship.—The electromyogram also serves as a valuable method of as the dose-response relationship. Electric may be visualized, after suitable amplification, by a cathode-ray oscilloscope or an oscillograph. Variations of the action potentials are detected by needle electrodes inserted into skeletal muscle. Normal muscle at rest shows no action potential, but muscle in severe spasm produces numerous action potentials. In addition to being a useful monitoring device in the management of severe reflex muscle spasm, electromyography is also an important research method in the study of effectiveness of various drugs in the management of the neuromuscular manifestations of tetanus (fig. 2).

Since the degree of hypertonia varies from time to time, constant electromyographic monitoring of the intravenous administration of methocarbamol is advisable. After an initial single dose (about 15 mg. per kilogram of body weight), the methocarbamol is best administered by continuous drip infusion in 500 cc. of 5% dextrose in water to maintain the desired suppression of reflex muscle spasm. The concentration used is determined by the electromyographic pattern.

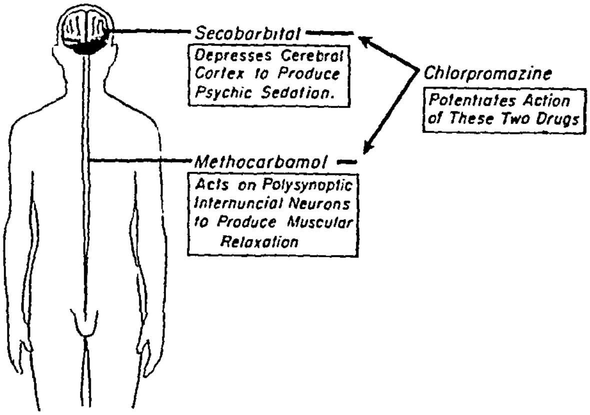
Secobarbital
Depresses Cerebral Cortex to Produce Psychic Sedation.
Chlorpromazine
Potentiates Action of These Two Drugs
Methocarbamol
Acts on Polysynaptic Internuncial Neurons to Produce Muscular Relaxation

Fig. 1.—Sedative-relaxant regimen for control of neuromuscular manifestations of severe systemic tetanus.

Adequate Pulmonary Ventilation.—The adequacy of pulmonary ventilation can be evaluated in terms of tidal volume and end-expiratory carbon dioxide concentration. A ventilation meter and infrared carbon dioxide analyzer have been used for this purpose. An approach has been made to the ventilatory needs of the individual patient through the application of the Radford nomogram.[9] Ve[illegible] insufficiency is manifested by an ele[illegible] periodic end-tidal carbon dioxide concen[illegible]son.
quacy of alveolar ventilat
of a mechanical res[illegible] Screening Examination
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The id[illegible] educational method for health pro-
mo[illegible] and preservation has been attempted only during the last two decades. The first cancer detec-

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edicine, Tulane University School of Medicine.

ideal. Electromyographic monitoring demonstrates the desired suppression of reflex muscle spasm. This is accomplished without mechanical assistance to maintain respiratory efficiency. Efficient pulmonary ventilation is maintained as indicated by determination of the end-expiratory carbon dioxide concentration and the tidal volume.

Rigid attention to pulmonary ventilation, the maintenance of a patent airway, and the aspiration of tracheobronchial secretions are important safeguards. In all cases of severe systemic tetanus, early tracheotomy should be performed. The presence of a tracheostomy halves the respiratory dead space and facilitates the prevention of secretional airway obstruction. The largest tracheostomy tube compatible with the size of the trachea should be inserted to minimize resistance to air flow. Thorough humidification of the inspired air helps keep tracheal secretions in a less viscous state and therefore more removable by coughing or suction. Humidification also helps prevent secretions from forming encrustations around the tracheostomy tube and within the trachea. An airway free of such encrustations has less resistance to ventilation. Under normal conditions, without tracheostomy, the inspired air arrives in the trachea at body temperature fully saturated with water vapor from the nasopharyngeal passages. This favorable state of saturation of tracheal air is difficult to approach in the tracheotomized patient because of the principles of relative humidity. Even if the air which is about to enter the trachea is saturated at room temperature,
it is bound to be less than saturated as it reaches
The temperature within the trachea. Therefore,
adequate fo. tinuous use of the best nebulizer is
indicated by the in keeping secretions liquid. Fre-
ried out in the routine mal saline solution into the
be carried out by the exam ded to supplement hu-
sician, as were biopsy and therap ally aspirate
amination included taking of a detail ented
history by an internist and also by a gynec
for the female patients, with use of a routine sup
plementary Cornell Medical Index History.[7] The
physical examination was complete, including a
rectal and genital examination for each sex and a

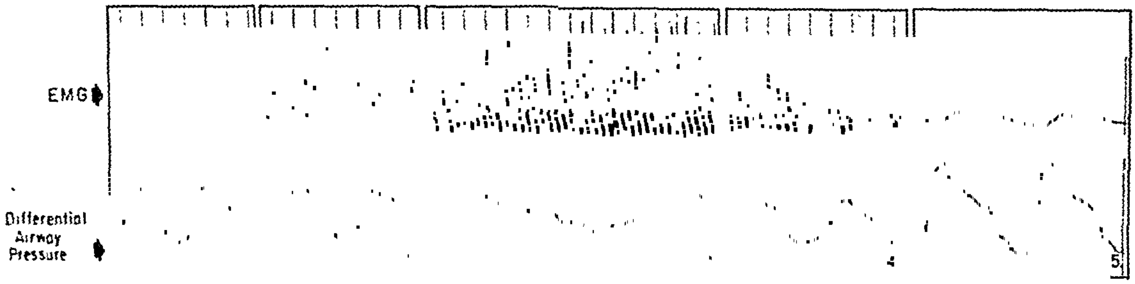

Fig. 2.—Electromyogram showing degree of reflex muscle spasm and dose-response relationship in sedative-relaxant regimen for severe systemic tetanus. Graphs show (1) normal control values, (2) moderate tetanospasm after moderate dose of strychnine, (3) severe tetanospasm after large dose of strychnine, (4) returning to normal one and one-half minutes after administration of methocarbamol, and (5) return to normal three minutes after administration of methocarbamol.

necessary to obviate the ever-present threat of regurgitation and aspiration. The normal cough mechanism can be effectively reproduced in the cooperative tracheotomized patient if the tracheostomy tube is momentarily occluded. If the patient is not cooperative, secretions must be removed by intratracheal suction at frequent intervals. The use of a Y-tube in the suction circuit permits the suction to be intermittently broken to minimize damage to the tracheal mucosa during suctioning. Suction should be performed rapidly and intermittently to prevent hypoxia, with a catheter long enough to reach deep into the major bronchi. Special emphasis is placed on constant, expert nursing care. A successful tracheotomy is absolutely dependent on meticulous after-care.

In addition to maintenance of a patent airway, adequate alveolar ventilation is necessary. The sedative, centrally acting, muscle-relaxant regimen has been successful, in our hands, in suppressing reflex muscle spasm without concomitant respiratory impairment. However, when a peripheral-acting muscle relaxant is used to prevent muscle spasm, respiratory depression is inevitable. Mechanical ventilation is required to insure proper tissue oxygenation and carbon dioxide elimination. Although several methods of providing mechanical ventilation are available, not all are practical. The tank-type respirator, as it is commonly used, is incompatible with a tracheotomy and greatly interferes with proper nursing and medical care. The cuirass respirator usually does not provide adequate ventilation for prolonged periods. Although the electrophrenic stimulation-type respirator preserves the normal intrathoracic pressure relations, its general use has been found to be impractical because of technical difficulties. The most effective of the mechanical respirators is one which creates intrapulmonary pressure changes to maintain ventilation. Such a machine may be coupled to a tracheotomy tube with an inflatable cuff.

The maintenance of effective ventilation by utiliz-
ing alterations in intrapulmonary pressure requires
ial precautions. The intrapulmonary pressure
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curve should be of the type causing the least possible impairment to right-heart filling to avoid a reduction in cardiac output with concomitant hypotension. The period of expiration should be of longer duration than inspiration so that compensatory hemodynamic readjustments may take place during this period of phasic decrease in intrapulmonary pressure. Tolerance of positive intrapulmonary pressure is dependent on the individual patient's ability to develop and maintain an elevated central venous pressure. During the phasic decrease in intrapulmonary pressure the elevated central venous pressure is important in permitting right-heart filling, and this contributes to the maintenance of a satisfactory cardiac output.

Thus patients with hypovolemia, peripheral vascular failure, and pharmacological sympathetic blockade tolerate injudicious pressure breathing poorly because of their inability to maintain a satisfactory central venous pressure. A system which alternates positive with negative pressure is less detrimental to the circulation than one which alternates positive with ambient pressure. However, recent evidence raises the question of the desirability of a negative phase, since it may be associated with reduced ventilatory efficiency due to air trapping in the terminal bronchioles.

The spasticity of the muscles of the tetanus patient decreases the thoracic compliance and opposes the maintenance of adequate ventilation. This undesirable state is improved by the use of skeletal muscle-relaxant drugs which facilitate pulmonary ventilation by decreasing spasticity and increasing thoracic compliance. Since the muscle tone is changing all the time, the variation in thoracic compliance enhances the problem of maintaining pulmonary ventilation by mechanical methods. The mechanical ventilators may require repeated readjustment owing to the variation in thoracic compliance. Without the anesthesiologist's constant interpretation of the changes in thoracic compliance and subsequent readjustment of the ventilator or the administration of the muscle relaxant, deleterious effects from excessive pressures or hypoventilation may develop.

General Patient Care.—The management of the patient with severe systemic tetanus is best carried out in an isolated room with special equipment. Constant care of these patients should be provided by trained nursing personnel under the surveillance of an anesthesiologist. Strict observation of vital signs, the efficiency of pulmonary ventilation, and the status of muscle tone is important, along with frequent tracheobronchial suction of secretions
majority of deaths from tetanus are du
quate or improper control of th
spasm and subsequent delete
phyxia.

Summary

Therapeutically sound regimens for the administration of antitoxin in the management of severe systemic tetanus have previously been formulated. Because, in the past, control of the neuromuscular manifestations without serious impairment of respiration or consciousness has been unsatisfactory, a sedative, centrally acting, muscle-relaxant regimen which approaches the ideal is advocated. This consists of administration of secobarbital (Seconal) or pentobarbital (Nembutal) for psychic sedation, methocarbamol (Robaxin) for skeletal muscle relaxation, and chlorpromazine (Thorazine) to potentiate the sedative-relaxant effect. Electromyographic monitoring together with determination of end-expiratory carbon dioxide concentration and tidal volume demonstrates adequate suppression of reflex muscle spasm without impairment of pulmonary ventilation. Special emphasis is placed on constant, expert nursing care, the prevention of secretional airway obstruction, and the maintenance of adequate alveolar ventilation. The anesthesiologist, with his knowledge of the pharmacological application of muscle relaxants and the physiological maintenance of pulmonary ventilation, can play a vital role in the management of severe systemic tetanus.

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The methocarbamol used in this study was supplied as Robaxin by the department of clinical research, A. H. Robins Co., Inc., Richmond, Va.

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INCIDENCE OF UNSUSPECTED "SHEEHAN'S SYNDROME"

HYPOPITUITARISM AFTER POSTPARTUM HEMORRHAGE AND/OR SHOCK–CLINICAL AND LABORATORY STUDY

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and
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Manifestations of hypopituitarism were looked for in 35 women who had survived postpartum hemorrhage and/or shock. Sheehan's syndrome probably represents one extreme of a spectrum of conditions resulting from damage to the hypophysis during hemorrhage and shock, and the purpose was to identify susceptible patients as the basis for preventive action. Eight case histories illustrate the complexity of the relationships found. Four women proved to have previously undiagnosed pituitary deficiency manifested by mammary and genital atrophy, amenorrhea, and sterility, with other characteristic symptoms and laboratory findings. No correlation was found between the severity of the postpartum hemorrhage and/or shock and the likelihood or degree of subsequent hypopituitarism, but the latter was found more frequently than had been expected. If it is watched for more carefully, more patients can be given the benefits of endocrine substitution therapy.

Anterior pituitary necrosis after postpartum hemorrhage and/or shock whose sequela is anterior pituitary insufficiency has acquired the name "Sheehan's syndrome," in contrast to pituitary insufficiency from other causes which is commonly called "Simmonds' disease." The typical syndrome is characterized by failure of lactation in the puerperium, amenorrhea, loss of axillary and pubic hair, genital and breast atrophy, superinvolution of the uterus, sterility, symptoms and signs of hypothyroidism, and various degrees of adrenocortical insufficiency. Less severe examples may include either isolated or various combinations of failure of anterior pituitary tropic hormones, i. e., gonadotropins, thyrotropin, and adrenocorticotropin. The disease is usually initiated shortly after the puerperium, becoming progressively worse after an interval of months, but it may not manifest itself for years. That pituitary insufficiency of a potentially lethal degree may exist in an apparently healthy subject was dramatically illustrated by the case reported by one of us and Conston.[1]

A 30-year-old patient, a gravida 5, para 4, had survived massive postpartum hemorrhage at the conclusion of her fourth pregnancy, with estimated blood loss of 1,500 cc., which resulted in shock lasting about two hours. During her fifth pregnancy she felt well, aside from excessive fatigue. Because she was diabetic a classic cesarean section was performed, with the patient under continuous spinal anesthesia. One minute after delivery she lapsed into a coma and died shortly thereafter. At autopsy about 85% of the anterior lobe of the pituitary gland was found replaced by necrosis, and the adrenal cortex was moderately atrophied. In retrospect [illegible]eehan's syndrome might have been suspected be- [illegible] failure of lactation, slow regrowth of pubic [illegible] The [illegible] taneous amelioration of the severity [illegible] adequate fo[illegible] tinuous after the postpartum hemor- [illegible] indicated by the [illegible] in keep[illegible] [illegible] ried out in the routine [illegible] mal sa[illegible] linical picture of an- be carried out by the exam[illegible] ded to vary considerably [illegible] sician, as were biopsy and therap[illegible] extremely [illegible] amination included taking of a detai[illegible] ally asp[illegible] de- history by an internist and also by a gynec[illegible] ented for the female patients, with use of a routine supplementary Cornell Medical Index History.[7] The physical examination was complete, including a rectal and genital examination for each sex and a

other survivors of postpartum hemorrhage and/or shock, however healthy they may appear on casual observation, might well be candidates for a similar catastrophe. It would be lifesaving to identify such persons so that their inability to withstand stress might be known and suitable prophylactic measures instituted. This study was designed to attempt such identification.

Methods and Procedures

Thirty-five survivors of postpartum hemorrhage and/or shock were evaluated clinically and 33 were subjected to a laboratory survey designed to estimate the function of the anterior pituitary and its target organs—the thyroid gland, the adrenal cortex, and the ovaries. These women were encountered in hospital or private practice, were sought out by a perusal of hospital records, or were referred by physicians who knew of our interest in this problem. [illegible]ng a[illegible] survey was repeated as often as possible in each [illegible]al pre[illegible] during the eight years of the study because fro[illegible] tendency of Sheehan's syndrome, in in practica[illegible] occasional cases, to manifest itself only after several years. A complete medical history was obtained from and physical examination performed on each subject, and laboratory studies were completed during the ensuing months. The laboratory methods we had outlined in a preliminary report[2] were only slightly modified and amplified over the years. Abnormal findings were verified by repetition whenever possible. Attempts to carry out an identical survey on a series of control patients were unsuccessful because of our inability to secure a large enough cooperative group.

TABLE 1.—*Significant Clinical Data in Thirty-five Survivors of Postpartum Hemorrhage and/or Shock*

Case No.	Age, Yr.	Interval Since Postpartum Hemorrhage/ Shock, Mo.	Severity		Duration Shock, Hr.	Transfusion, Cc.	Hysterectomy	Moribund	Lactation
			Hemorrhage	Shock					
			Sheehan's Syndrome						
4	27	132-141	+	Unknown	Unknown	0	No	No	Normal
5	50	288-336	++++	++++	Unknown	"Many"	No	Unknown	Absent
18	36	12-13	++++	++++	4	2,500	No	No	Poor
35	42	221-229	++++?	Unknown	Unknown	8,000?	No	Unknown	Unknown
			Equivocal						
13	40	1-37	+++	++++	24	2,000	No	Unknown	Unknown
33	33	5-36	++++	++++	12	4,500	Yes	Yes	Absent
7	33	4½-60	++++	++++	2	2,500	No	No	Unknown
36	26	12	++	++	2	1,500	No	No	Poor
			Normal						
2	36	14-84	++++	++++	6	"Many"	Yes	Yes	Absent
12	30	72-114	++++	++++	6-7	3,500	No	No	Absent
17	32	9-48	++++	++++	6-8	5,000	No	No	Normal
34	33	15	+++	++++	5	2,000	No	Yes	Normal
29	49	252	++++	++++	3+	650	No	?	Normal
1	47	1-72	++++	++++	2+	6,500	Yes	No	Reduced
3	24	3-64	0	+++	2	1,000	No	No	Normal
23	32	8-9	+++	+++	2	5,500	No	?	Normal
24	28	27	+	++++	2	1,000	No	No	Normal
19	46	120	++++	++++	1+	1,500	No	No	Normal
28	28	31	++++	++	45 min.	750	No	No	Unknown
6	43	24-80	++++	++++	30 min.	3,500	No	Yes	Normal
11	28	1-24	++++	+	30 min.	11,500	Yes	No	Normal
21	33	50-57	++++	+++	15 min.	4,000	Yes	No	Normal
26	37	15-21	0	++	15-20-min.	2,500	No	No	Unknown
22	24	38	++	++	10 min.	1,000	No	No	Normal
25	33	60	++++	+	5 min.	3,250	Yes	No	Unknown
8	23	24-87	++++	++++	Many	2,500	No	Yes	Normal
10	31	120-129	++	?	Unknown	Several	No	No	Normal
14	34	132-184	+++	++++	Many	"Many"	No	No	Poor
15	35	60-96	++++	Unknown	Unknown	3,500	No	No	Normal
16	31	24	+	0	0	0	No	No	*
20	33	24-48	++++	++++	Unknown	Unknown	No	No	Unknown
27	32	168	++++	++++	Unknown	1,000	Yes	Yes	Unknown
30	23	60	+++	++	Unknown	500	No	No	Unknown
31	30	180	++++	++++	Unknown	"Many"	No	Yes	Absent
32	25	5-18	0	++	Unknown	1,000	No	No	Unknown

* Chiari-Frommel syndrome.

Results

The significant clinical data of the 35 subjects are shown in table 1; the laboratory results for 8 of the 35 women are outlined in table 2. The remainder of the data, which consist of the laboratory results of the "normal" group, have been omitted to cons space. Four patients showed sufficient cli laboratory abnormalities to warrant anterior pituitary insufficiency

drome. The diagnosis of Sheehan's syndrome was interpreted in its broadest sense, i. e., to include any detectable degree of hypopituitarism, and does not necessarily imply "panhypopituitarism" or total loss of anterior pituitary function. Isolated, partial, or selective pituitary failure[3] may occur, causing failure of production of one or more, but not all, of the recognized pituitary tropic hormones, i. e., gonadotropins, thyrotropin, and adrenocorticotropin.

Report of Cases of Sheehan's Syn

CASE 4.—A 27-year-old wo
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The distribution according to age and sex of the patients treated by transurethral operation is listed in table 2. It can be seen that well over one-half of these operations occurred in the seventh, eighth, and ninth decades of life. The incidence of degenerative disease of other organs and tissues, of course, is high in these decades. The mean average age was 62.6 years.

TABLE 2.—*Age and Sex of Patients with Vesical Neoplasm Treated by Transurethral Removal, Fulguration, and Electrocoagulation*

	Total Patients		Male		Female	
Age, Yr.	No.	%	No.	%	No.	%
30-39	10	1.9	10	2.3	..	..
40-49	49	9.4	37	8.6	12	13.3
50-59	138	26.5	113	26.2	25	27.8
60-69	199	38.2	174	40.4	25	27.8
70-79	107	20.5	83	19.3	24	26.7
80+	18	3.5	14	3.2	4	4.4
Total	521	100	431	100	90	100
Mean age	62.6 yr.		62.5 yr.		63.1 yr.	

Table 3 shows that in more than one-fourth of the cases in which transurethral methods were used the patients were found to have high-grade lesions.

TABLE 3.—*Grade of Malignancy of Lesions of Bladder Treated by Transurethral Removal, Fulguration, and Electrocoagulation*

	Patients	
Grade	No.	%
1	246	47
2	131	25
3	115	22
4	29	6
Total	521	100

It is interesting to notice (table 4) that the ratio of the preponderance of the lesion in the male is greater than 4 to 1, indicating that females are more resistant to the development of vesical neoplasm and that they also survive longer, once the disease has developed. No female less than 40 years old was found to have a tumor. ✓

TABLE 4.—*Five-year Survival Rates According to Sex of Patients Treated for Vesical Neoplasm by Transurethral Removal, Fulguration, and Electrocoagulation*

	Patients		Lived 5 Yr. or More Postoperatively	
	Total	Traced	No.	%*
[illegible]	431	406	228	56
[illegible]	90	84	52	62
[illegible]	[illegible]	490	280	57

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The [illegible] adequate fo[illegible] indicated by the [illegible] ried out in the routine [illegible] be carried out by the exam[illegible] sician, as were biopsy and therap[illegible] amination included taking of a detai[illegible] history by an internist and also by a gynec[illegible] for the female patients, with use of a routine supplementary Cornell Medical Index History.[7] The physical examination was complete, including a rectal and genital examination for each sex and a

bladder. Actually, many die of other conditions. In most cases the tumor has been controlled and cancer is not the reported cause of death.

Survival rates computed according to the grade of the tumor and the type of operation performed are shown in tables 6 and 7. Of the 521 patients who underwent transurethral methods of operation, 57.1% lived or were still living from 5 to 10 years postoperatively.

TABLE 5.—*Five-year Survival Rates According to Age of Patients Treated for Vesical Neoplasm by Transurethral Removal, Fulguration, and Electrocoagulation*

	Patients		Lived 5 Yr. or More Postoperatively	
Age, Yr.	Total	Traced	No.	%*
<50	59	56	45	80
50-59	138	126	90	71
60-69	199	193	107	55
70+	125	115	38	33
Total	521	490	280	57

*Based on traced patients. Inquiry as of Jan. 1, 1959.

Reference to table 8 shows that total cystectomy and suprapubic resection were not performed exclusively for the 115 patients with high-grade neoplasms; these operations also were performed on 27 patients with low-grade tumors. During the same time interval transurethral methods were used in 144 patients with high-grade tumors (table 6).

TABLE 6.—*Five-year Survival Rates, According to Grade of Malignancy; Patients Treated for Vesical Neoplasm by Transurethral Removal, Fulguration, and Electrocoagulation*

	Patients		Lived 5 Yr. or More Postoperatively	
Grade	Total	Traced	No.	%*
1	246	229	168	73
2	131	121	71	59
3-4	144	140	41	29
Total	521	490	280	57

*Based on traced patients. Inquiry as of Jan. 1, 1959.

The five-year survival rate was 19.8% for patients who underwent cystectomy and 24.4% for those who underwent suprapubic resection (table 7).

TABLE 7.—*Five-year Survival Rates of Patients with Vesical Neoplasm According to Type of Operation*

	Patients		Lived 5 Yr. or More Postoperatively	
Operation	Total	Traced	No.	%*
Total cystectomy	91	81	16	19.8
Suprapubic resection	51	45	11	24.4

*Based on traced patients. Inquiry as of Jan. 1, 1959

Comment

In accumulating data on results of operation the number of patients who survived for a stated period is not so important as is the question of how much relief was obtained for some and how little for others. The person who has a small lesion of identi[illegible]ing a histological pattern can expect, and of course [illegible] derive, considerably more benefit than the fro[illegible] in practica[illegible] one who procrastinates or who, through no fault of his own, finally appears when the bladder is infiltrated with cancer of a high grade. Yet, in the analysis of the total series, all patients in all sorts of conditions are placed together; hence, comparison of series or groups is of little real worth. The lesson clearly evident from a study of any considerable number of cases unquestionably is that early diagnosis and a prompt and inclusive effort at cure are of paramount importance. One cannot stress too often the physician's obligation to regard the finding of hematuria, either gross or microscopic, with real and sufficient concern. This is the message that urologists must carry to the family physician, for he is the first confidant of the patient who has witnessed, and rightly become concerned by, the appearance of blood in his urine. If the patient complaining of hematuria is referred for study, he will have the benefits of early diagnosis of the tumor, and, in turn, prompt and properly selected remedial measures may result in a cure.

Unfortunately, in spite of the best efforts, failure sometimes will result, but failure is not a good reason for abandonment of all hope. Too often disconsolation is the attitude of both the patient and the physician whom he first consults. Such defeatism must be corrected if the prognosis accompanying vesical neoplasm is to be improved. And this prognosis can be improved, beyond any doubt. The tools for diagnosis and therapy are available; let us hope that they will be used more efficiently by more and more practitioners.

TABLE 8.—*Distribution of Cases of Vesical Neoplasm According to Grade of Malignancy*

	Total, Cystectomy		Suprapubic Resection	
Grade	No.	%	No.	%
1	2	2.2	4	7.8
2	13	14.3	8	15.7
3	54	59.3	29	56.9
4	22	24.2	10	19.6
Total	91	100	51	100

MEDICAL PROGRAM OF WELFARE AND RETIREMENT FUND OF THE UNITED MINE WORKERS OF AMERICA

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Adequate medical care for miners and their families was virtually unobtainable before the establishment of the welfare and retirement fund here described. Many administrative problems had to be solved, but relations with most physicians in the mining areas of the 26 states in which the program now operates are cordial and satisfactory. Formerly most patients had to be content with the physician employed by the company or with other physicians whom they could afford to pay within a distance they could afford to travel. Now they can be transported to distant medical centers when necessary, and the beneficiary has a wide choice from the many physicians whom the fund pays for services. The fund has made the most phenomenal strides ever seen in improving the medical services available to its beneficiaries.

I am grateful for this opportunity to tell you the facts about the medical program of the United Mine Workers of America (UMWA) welfare and retirement fund—the reasons for its existence, the spirit in which it was planned, and the course which it has followed from its beginning in 1948 until the present.

I assume that for the purposes of this paper the reader will accept as facts that the mining of coal has always been a hazardous industry and that, prior to the establishment of the fund, adequate health and medical care for the miners and their families was, for the most part, unobtainable. Documented reports of surveys and a mass of published material are readily available to those who may wish to inquire further.

Origin of the Fund

The trust agreement established by the national bituminous coal wage agreement of 1950 created the United Mine Workers of America welfare and

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Executive Medical Officer, United Mine Workers of America.

Read before the Section on Preventive Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

retirement fund, pursuant to the Labor-Management Relations Act of 1947, as an irrevocable trust to be located in Washington, D. C. The trust fund superseded the previous 1947 UMWA welfare and retirement fund, which was merged with the present fund on its establishment in 1950 and operates in conformity with the trust agreement as amended Sept. 29, 1952.

Administration.—In conformity with terms of the trust agreement and with federal statutes governing trusts, the fund is organized and administered as a separate entity, independent of both the union and the coal operators, pursuant to regulations adopted by its board of three trustees designated in accordance with the trust agreement.

Financial Aspects.—Trust fund revenues derive from monthly royalty payments on each ton of coal produced for use or for sale, which the trust agreement obligates all signatory operators to make directly to the office of the trust fund. The royalty payment at the present time is 40 cents per ton. Title to all such money paid into, or due and owing, the fund is vested in and remains exclusively with the trustees of the fund. Operations of the trust fund are on an industry-wide basis, and its authorized benefits reach beneficiaries in 26 coal-mining states.

The benefits provided by the trust fund are authorized by the trustees. The trustees have full and final authority to revise, suspend, or terminate the benefits at any time. The trust fund pays the entire cost of all the benefits it provides. No contributions or payments of any sort by miners are, or ever have been, made to the trust fund.

Scope of Benefits

At present, benefits authorized consist of pension benefits, hospital and medical care benefits, widows' and survivors' benefits, and mine disaster benefits. Eligibility for trust fund benefits is determined by the trustees in conformity with the terms of the trust agreement. There are presently about one million potential beneficiaries, bituminous coal miners—working, retired, and unemployed—and their wives, dependent children, and certain other eligible dependents.

In conformity with regulations of the trustees, these hospital and medical care benefits are made available to the extent and in the manner determined by the director of the fund through the medical, health, and hospital service. This professional service, under the administration of the fund's executive medical officer, has full and final powers of decision over the physicians and hospitals for whose services trust fund payments will be made. The program as it stands today is that which we physicians in the fund, and the medical profession concerned with the care of our patients, have combined to make it. The only obligation which the trustees and the director of the fund have ever placed on the medical administration is to insure that the medical and hospital services for which the money is provided are of the highest quality obtainable and that the cost is reasonable and necessary according to professional standards.

Because of the hazardous character of coal-mining operations, and the places in and conditions under which the work is carried on, the medical benefits are designed as far as possible to provide the services which the beneficiaries need the most. They cover the entire cost of hospitalization and medical care in the hospital, regardless of how old the beneficiary may be, how often or how long he must be hospitalized, or the length of time the condition may have existed before his eligibility for benefits was established. Payment is made for specialists' services whether or not the patient is hospitalized, and beneficiaries are sent for any distance that may be necessary for care by the best specialists and in the best medical centers of the country, when the kind of treatment they require cannot be furnished otherwise.

Among the institutions to which hundreds of our patients have been sent for special care and treatment are the New York University Institute of Physical Medicine and Rehabilitation; the Kessler Institute of Rehabilitation; the Wisconsin Neurological Foundation; the George Washington University, Massachusetts General, and Johns Hopkins hospitals; the Vanderbilt University, Duke University, and University of Pennsylvania medical centers; the Mayo, Ochsner, and Cleveland clinics; and the National Institutes of Health.

Limitations.—Trust fund payment is not authorized for services for which a beneficiary is eligible by official agencies such as the Veterans Administration, Workmen's Compensation, vocational rehabilitation agencies, state institutions for the care and treatment of tuberculosis and mental diseases, state crippled children's programs, or state public health departments, nor are payments authorized for services which voluntary organizations, financed locally and supported in part by contributions from the coal miners, may rightfully provide. Rather than duplicate their services and diminish their support, cooperative relationships are developed. This tends to strengthen the participating agencies and augment their fields of usefulness. Our cooperative relationships with the American National Red Cross and the National Foundation, for example, have been of great assistance to those who are served and to our respective agencies as well. Trust fund payment is not authorized for hospital or medical services when the cost of such services is the responsibility of a third party.

Relations with Physicians and Hospitals

In planning for services to the beneficiaries, the medical staff of the fund placed its main reliance on the physicians and hospitals in and around the mining communities. We undertook to make mutually satisfactory arrangements with any reputable physician who expressed a wish to serve our patients, and our beneficiaries were free to choose any physician with whom arrangements had been made. We likewise made arrangements with the various hospitals on an individual basis, because they differed widely in the type of service they could render. We authorized the physicians to hospitalize our beneficiaries at our expense and relied on them to exercise this privilege only for patients whose illnesses could not be treated adequately in the office, outpatient clinic, or home.

We authorized and encouraged the physicians to refer our beneficiaries to qualified specialists for consultation, diagnostic service, and treatment, when indicated, all at fund expense. When necessary, specialists may be brought to out-of-the-way localities to examine groups of patients in consultation with their family physicians and advise as to treatment. Thus have many thousands of patients and their physicians been greatly benefited.

It has been our purpose to be fully informed of the quality of care that can be rendered in each hospital, and, if necessary, to cooperate and assist in developing and maintaining standards based on the knowledge and experience of competent authority. This has resulted in great improvements in local hospitals and many have been accredited or are ready for inspection for accreditation wholly or in part because of the incentive provided by the fund. We arranged to pay any physician whom a beneficiary may select for emergency or other services while he is living or traveling outside of the coal-mining areas. We require only that these physicians and hospitals notify us in advance, when possible, so that a satisfactory understanding can be reached.

Since all that the fund has ever desired or asked is that the highest quality of care obtainable be rendered to its beneficiaries and that the cost be reasonable and necessary according to professional standards, we believed that the medical profession throughout would help us toward this end. The understanding and cooperation of organized medicine were therefore sought early at the national, state, and local levels.

Neither the physicians who were to render the service nor the fund which was to pay could foresee all of the problems that would arise or the adjustments that would have to be made to resolve them. It was our fervent hope and expectation, however, that organized medicine and the medical service of the fund, working together in a united effort, could iron out whatever difficulties might be encountered, gradually develop a pattern of medical care that would insure high quality without unnecessary costs, and serve as a model that other programs might follow to the satisfaction and advantage of everyone concerned.

Our relationships with most physicians in the mining areas of the 26 states in which our program operates have always been cordial and satisfactory and continue to be so at present. In fact, they have grown progressively better as physicians have learned, through their experience, of our soleness of purpose in obtaining good medical care at fair cost and of the integrity with which the program is conducted. Were it otherwise our patients would not now be receiving the full amount of service possible under the benefits authorized, nor would the standards of medical and hospital care in the mining areas be steadily advancing.

During the formative years of our program the Councils on Medical Service and Industrial Health of the American Medical Association and the A. M. A. Committee on Medical Care for Industrial Workers gave valuable assistance in surveying problem areas in the coal fields, arranging conferences with representatives of state and local medical societies, and endeavoring to resolve the problems that were bound to be encountered. A number of the state and county medical societies were also most cooperative and continue to operate on a basis of mutual understanding, respect, and cooperation.

As the program developed, however, we were confronted with problems of unsatisfactory services and costs that could not be resolved, under what we found to be the unrealistic provision of permitting any physician to hospitalize all the beneficiaries he wished, at the expense of the fund, and paying him for any service he saw fit to perform, with the hospitalization continuing for any length of time he might determine. The only effective recourse from this impractical method of operation was to select the physicians whom the fund would pay for the services it authorized.

When this procedure was put into effect, the problems and difficulties which were previously encountered largely disappeared, and our relationships with the thousands of physicians who serve our beneficiaries everywhere have continued on a cordial, friendly, and cooperative basis.

Choice of Physician

The term "free choice of physician" has not been adequately defined. It is subject, therefore, to almost any interpretation that a person or group may wish to place on it. It may then be used for any purpose, commendable or otherwise, that may be desired. Too often it serves as a rallying cry to awaken an emotional response without understanding or recognizing the facts. This, in turn, may lead to ill-considered actions which would not eventuate if logic and reason were enabled to prevail. I believe that this is at the root of most of the controversy which has been engendered in certain state and county medical societies in relation to the medical program of the fund.

I am confident that many grievous actions could have been averted and that a large amount of wasted time could have been devoted to the furtherance of better understanding and cooperation if the truth were recognized that the fund is in fact contributing to the support and implementation of "free choice of physician" in a most effective manner, provided the interpretation of the term is according to the rule of reason.

Before the medical program of the fund came into existence there was virtually no choice of physician by the people who are now its beneficiaries. The working miners and their families in many places had no choice other than the camp physician employed by the company, whom the miners paid for services received. There were seldom any other physicians whom they could afford to pay within a distance they could travel.

Unemployed and disabled miners without an income had no choice other than that of a physician who would accept them free of charge for such limited treatment as he could afford to offer. If they were compelled to seek their medical care through public assistance agencies, they had no choice other than that of the physician employed by the agency.

Contrast this situation with the free choice of physician which now prevails through the medical benefits which the fund has made possible. Instead of one physician the beneficiary now has a wide choice from the many physicians whom the fund pays for services. More than 7,000 physicians were paid by the fund during the past year. In many mining communities the fund at present pays any physician whom a beneficiary may choose. In other communities he has free choice from among a majority of the physicians who desire to serve beneficiaries. If necessary, a beneficiary may be referred to any one of a large number of specialists with whom the fund has made arrangements. Beyond this, he may be transported at the expense of the fund to one or another of the great medical centers of the country where a team of physicians, if necessary, will be paid by the fund to provide the highly specialized care that an individual patient may require.

During the past 10 years the fund has made direct payments to many thousands of physicians of over 120 million dollars. Its payments to hospitals have amounted to more than 180 million dollars. More than 500,000 beneficiaries have received medical care as hospital inpatients. In addition, over 8 million office and outpatient clinic visits to specialists for diagnosis and treatment were paid for by the fund.

It would seem that, by increasing the free choice of physicians from a few hundred to many thousands, and by placing no limit on the extent to which the highest quality of service will be provided, the UMWA welfare and retirement fund has qualified under terms of fairness and justice as a leading collaborator in recognizing the value and expanding the scope of free choice of physician. It is obvious that instead of tending to lower the quality and availability of medical care to its beneficiaries, as certain medical society resolutions assert, the complete opposite is true. The fund has made the most phenomenal strides that have ever been known in raising the quality and extending the availability of medical services to its beneficiaries.

Cooperation of Physicians.—Throughout the years of its existence the fund has dealt with thousands of physicians who have served its beneficiaries well. They have provided high-quality care, coupled with a devoted interest in the personal needs and problems of the miners and their families.

Many of these unselfish physicians share the frugalities and difficulties of living in remote communities as neighbors to their patients and their families. This they do without complaint. Others are consultants who travel many hard miles to bring their skills and talents to the ill. We owe much also to the physicians in the great hospitals and medical facilities of the large cities who extend understanding, encouragement, and hope to the beneficiaries we send to them with some of the most serious and complex problems they have ever seen.

Many of these physicians have suffered abuse and criticism and have been hampered in their work by less understanding colleagues, because they believed in the fund's objectives and continued to serve its beneficiaries, without regard to controversial issues and with a desire only to help their fellow man. To all of these men and the indispensable work that they are doing, the fund and its beneficiaries are profoundly grateful.

907 15th St. N. W. (5).

PROGNOSTIC AND THERAPEUTIC IMPLICATIONS OF POLYPS IN METACHRONOUS COLIC CARCINOMA

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In recent years increasing attention has been paid to the problem of so-called metachronous or asynchronous carcinoma of the colon, a condition represented by a distinct, new primary colic neoplasm arising after successful resection of an original, separate primary carcinoma. The greater awareness of this entity may be a result of the greater natural longevity of the population and the marked improvement in our operative mortality statistics; the increased life span allows a patient to survive longer to acquire a new primary lesion of the colon. Previously Ewing[1] believed that the development of one carcinoma was a safeguard against the appearance of another, and for many years his teaching prevailed. As recently as 1930, Lockhart-Mummery[2] felt that the presence of one neoplasm conferred a great degree of immunity against the development of a new lesion. Nevertheless, there were isolated reports in the literature, such as that of Peck[3] in 1924 of the incidence of one metachronous carcinoma in a series of 69 colic resections for carcinoma. It was not until 1938, however, that Brindley[4] cast a shadow of doubt on the former concept with his publication of 306 cases of colon resection for carcinoma among which were 2 cases of metachronous carcinomas, occurring at intervals of four and seven years respectively. Subsequently there have been several reports referring to this phenomenon; some of these are listed in table 1.

Our interest in this problem was stimulated by several recent patients who had had resections of the colon for carcinoma and who returned with new primary lesions of the colon. It is all the more disillusioning to note this condition in this group of patients since it has long been recognized that carcinoma of the colon carries with it a better prognosis than most neoplasms, other than those of the skin. Nevertheless, here we had a group of patients who had been ostensibly cured of their original disease only to have their lives again placed in jeopardy by another similar lesion. Consequently, we decided to analyze those patients with metachronous carcinoma and determine if there was any factor common to the group which might serve to lead us to the finding of a "sentinel" sign. This sign would then be used as a prognosticator for metachronous carcinoma of the colon, i. e., if present, it would indicate that the possibility for the development of a new carcinoma was great.

A neoplasm is called metachronous if it arises as a distinct, new, primary growth after the supposedly complete removal of a similar neoplasm. The frequency of metachronous carcinoma of the colon was investigated in a series of 1,628 patients who underwent resections for primary carcinoma of the colon during a 10-year period. In 1,100 of these cases removal was considered satisfactory and an excellent prognosis was given, but among them were 49 cases of double carcinoma and 4 of triple carcinoma. Of 77 patients who developed new lesions, 3 had had more than one carcinoma at the time of the original operation. One patient had three separate laparotomies for independent colic carcinomas. Data on the location of the lesions and their relation to polyps convince the authors that, whenever true adenomatous polyps are noted in the immediate vicinity of a carcinoma of the colon at operation, a radical procedure, such as subtotal colectomy, should be performed.

Material and Methods

In the 10-year period from Jan. 1, 1949, to Dec. 31, 1958, 1,628 resections for carcinoma of the colon were performed at the Mount Sinai Hospital, on both private and ward services. This figure does not include cases of ulcerative colitis or familial polyposis, since the latter lesions present problems peculiar to their disease and are still the subject of much discussion in themselves. Inasmuch as our prime concern was to discover a clue as to the possible future development of a second carcinoma, the important studies concerned those patients in whom curative surgery was attempted at the time of the first resection. There were 346 patients who were either inoperable, died in the immediate postoperative period, or had palliative resections and died of their disease within a year. An additional 182 patients showed evidence of local or distant spread, making cure of the disease impossible or, at best, unlikely. Of this latter group, 101 were followed up until their death within five years in 93 cases and for up to seven years in the remaining 8 cases. Thus, 32.4% of the total group of 1,628

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patients would not have been considered candidates for any further therapy, regardless of associated findings, since their primary disease or general condition would have precluded this. Hence we are left with 1,100 patients who, when seen at the first operation, were given an excellent prognosis. Of this group 453 (41.2%) have been followed up for three months to 28 years.

TABLE 1.—*Reported Cases of Metachronous Carcinoma of Colon*

Author	Total Cases	Metachronous Neoplasms, No.
Berson and Berger, Surg. Gynec & Obst 80:75-84 (Jan.)	344	5
Thomas and others, 1918[5,6]	4,400	37
Lillehei and Wangensteen, 1955[6]	43	5
Ginzburg and Dreiling, 1956[7]	700	25
Beal and Cornell, Ann. Surg. 143:1-7 (Jan.) 1956	140	8

In most cases, the length of the resected specimen is noted in the pathology report, as is the size of the lesion, the presence or absence of other lesions, and the presence of polyps. In addition, it is possible to tell in most cases how much normal intestinal tissue is present on either side of the carcinoma. Usually there is a note on the patient's chart as to the preoperative roentgenographic findings, although in many cases the actual official report is not present.

Metachronous Carcinomas

There were 77 patients who had two or more colic resections for separate, independent, primary carcinomas of the colon, or 4.7% of the total group. However, these 77 represent 7% of the 1,100 patients who were considered potentially curable at the time of their first resection and 17% of the group of 453 patients that has been followed up. Twelve of these patients had their first procedure at another hospital, and the record is either missing or incomplete; the record of one patient who was operated on at this hospital the first time is missing; two patients had rectal carcinomas which were fulgurated and, therefore, there is no resected specimen; and one patient had a sigmoid polypectomy for carcinoma, at which time the operative note made no mention of further exploration. Thus, in 16 of the 77 cases of multiple colic resection the record of the first procedure is either missing or inadequate. One patient had his second procedure at another hospital; one patient signed out against advice of his physicians while awaiting his second operation and subsequently died without being operated on; two patients died in the hospital while awaiting their second operation; and eight patients had lesions considered unresectable at the time of their second laparotomy. Therefore, in 12 of the 77 patients with multiple resection there is no pathological specimen for the second carcinoma. It is interesting to note that one patient had three separate colon resections for new, primary colic growths.

Findings

It was thought that preoperative roentgenograms might reveal lesions such as the carcinoma itself or polyps which may have been missed originally, but in reviewing the films that were available and official reports of those that were not, it became immediately apparent that no clue to the possible development of a new lesion or even its original presence could be found. In most cases where polyps were present in the resected specimen in addition to the primary carcinoma they were not evident on the roentgenographic film, nor were some of the double and triple carcinomas. This is in accord with the findings of others. Deddish and Hertz,[5] at operation on 103 patients, discovered polyps not revealed by roentgenogram in 46.6%. Forty per cent of these polyps were over 1 cm. in diameter. Furthermore, 47% of 32 patients who had had resection for carcinoma had additional lesions.

Table 2 depicts the locations of both types of lesions, and it can be readily seen that there is essentially no difference between the location of the lesions in the group that later developed new neoplasms and the total group. It is not surprising that there is a higher incidence of lesions in the middle of the colon at the time of the second resection, since the areas with the highest rate of occurrence had already been resected in many cases. This also indicates that, although the incidence of neoplasms of the transverse colon is generally lower than that of the rest of the colon, the neoplastic potential is still great if given the opportunity to arise. It will be noted that the age distribution at the time of the appearance of the first lesion is similar to that for the general population of colon carcinomas (table 3).

Lymph nodes positive for carcinoma were found in 663 of the total group and in 18 and 19 of the group with metachronous carcinomas at the time of the first and second procedures respectively. This incidence is not surprising because those without positive nodes had a greater chance of surviving to develop another lesion. However, at the time of the second occurrence of colon carcinoma the situation was greatly altered, for six patients had distant metastases and eight had unresectable lesions. This fact certainly emphasizes the need for preventing the occurrence of another potentially lethal lesion,

TABLE 2.—*Locations of Carcinomatous Lesions in Series of Colonic Resections*

Area	Total Group Without Metachronous Group (1,628 Patients)	Resections in Metachronous Group (77 Patients)	
		First	Second
Ascending colon	307	12	7
Hepatic flexure	38	5	10
Transverse colon	57	5	15
Splenic flexure	64	4	7
Descending colon	110	4	9
Sigmoid colon	631	40	25
Rectum	344	12	14
Total	1,685	82	87

for 14 (18%) of the 77 patients who had two or more resections were then seemingly incurable of their disease.

As can be seen from table 4, more than half of the 77 patients returned with a new lesion in less than 5 years, i. e., 42 patients; 21 reappeared from 5 to 10 years later; and in 15 patients a new lesion occurred more than 10 years later. In one case it was 26 years and in another 27 years before the patient reappeared with a new colonic lesion. It is entirely possible that those patients who were discovered to have a new lesion less than one year from the time of the first resection actually had had a synchronous carcinoma which had been missed at the time of the first operation. Although there is no way of definitely ascertaining this, the proposition that a patient could reappear four months after a resection for colonic carcinoma with a second primary lesion which was not there originally seems difficult to accept.

TABLE 3.—*Age Distribution in Metachronous Group of Cases of Carcinoma of Colon*

Age, Yr.	Patients, No.
20-29	1
30-39	3
40-49	10
50-59	25
60-69	25
70-79	8
80-89	5

In the group of 1,100 patients considered potentially curable at first resection, exclusive of those with subsequent new lesions, there were 49 cases of double carcinoma and 4 cases of triple carcinoma. Of the 77 patients with new lesions, 3 had more than one carcinoma at the time of the original procedure. Thus at least 12% of the 1,100 patients had at least two carcinomas. There were two instances of three lesions: the first with two lesions in the right side of the colon and one in the left, and the second with one lesion in the right side of the colon and two in the left; one patient had two lesions on the right side of the colon. All three patients had several polyps in the resected specimens, in addition to the carcinomas. By the time of the second procedure, however, one patient had six carcinomas from the cecum to the sigmoid; one had three carcinomas; and five patients had two carcinomas. As noted above, one patient had three separate laparotomies and resections for independent colic carcinomas.

TABLE 4.—*Time Interval Between Occurrence of First and Second Carcinomas of Colon*[*]

Yr., No.	Cases, No.
0- 1	5
1- 2	8
2- 3	13
3- 4	10
4- 5	6
5- 6	6
6- 7	2
7- 8	6
8- 9	4
9-10	3
10-11	6
11-20	7
21-30	2

[*] Range: 4 mo. to 27 yr.

Table 5 represents an analysis of the incidence and location of the adenomatous polyps discovered in association with the primary carcinoma. These polyps, ranging in size from 2 mm. to 5 cm., with an average of 2 cm., were all considered true adenomas; papillomas and mucosal excrescences were not considered in this analysis. As mentioned above, cases of familial multiple polyposis were excluded, as were the pseudopolyps of ulcerative colitis. Of 341 patients who had polyps in association with their carcinomas, 91 were considered incurable at the time of their original laparotomy. As was the case with the entire group of patients, one may again consider as pertinent to the problem of metachronous carcinoma only those 250 patients who would have been considered for further therapy. Of these, 98 (39.2%) have been followed up for periods of three months to 28 years. It is from this last group that 30 patients with polyps in the original specimen and subsequent metachronous carcinomas have been drawn. Thus, 30.6% of all patients with polyps who were considered curable originally and have been followed up have returned with at least one new independent, primary carcinoma of the colon. Furthermore, these 30 patients represent 49% of the 61 patients with metachronous carcinoma for whom we have a record of a resected specimen at the time of the first procedure. Of two of these patients who also had unsuspected carcinomas in polyps in addition to the main lesion, one had two such lesions and the other one.

TABLE 5.—*Analysis of Adenomatous Polyps Discovered in Association with Primary Colic Carcinoma*

Incidence	
Polyps in total group	341
Polyps in metachronous group	
First resection	30
Second resection	13
Location	
Less than 1 cm. from main lesion	14
1-6 cm. from lesion	7
7-12 cm. from lesion	3
More than 12 cm. from lesion	2
Not stated	4

In addition to 30 instances of findings of polyps in the first resected specimen, 13 additional patients had polyps at the time of the second resection. It is possible, although improbable, that none of these 13 had polyps present at the time of the original procedure. However, if we take the total number of patients with polyps at either the first or the second procedure, we have 43 (56%). It is also apparent that 21 of the 30 specimens included polyps within 6 cm. of the main lesion and 24 of the 30 had polyps within 12 cm. of the lesion. It would appear, therefore, that we can correlate the incidence of adenomatous polyps associated with a primary carcinoma with the subsequent appearance of a separate, independent, primary carcinoma of the colon in a relatively high percentage of cases.

Comment

In 1948, Thomas and co-workers [6] found an incidence of 44.5% of adenomatous polyps among their 37 cases of asynchronous carcinomas of the colon, whereas, in the entire series of more than 4,000 cases of colon carcinoma, the incidence was only 20%. Lillehei and Wangensteen [7] found that, among 43 patients who had a subtotal or total colectomy for a carcinoma of the descending colon, there were 3 instances of a second carcinoma and an incidence of 22 (51.6%) with associated polyps. There are only two other cases where the incidence of associated polyps is mentioned in regard to metachronous carcinoma. Ginzburg and Dreiling [8] found four instances of associated adenomas at the time of the first resection and three at the second, in two of which polyps had been present in the first specimen resected. Other authors make no specific mention of the incidence of polyps associated with metachronous carcinoma.

Much has been written on the question of the malignant potential of adenomatous polyps and the subject is still far from settled. Although it is not our purpose to resolve this question, it is a pertinent one with respect to possible prophylaxis for metachronous lesions. Regardless of whether the over-all population with colonic and rectal adenomas is harboring precancerous lesions, a small but definite percentage of these persons apparently have a greater tendency to develop frank cancer of the colon than the rest and, moreover, a good number of these persons have a sufficient malignant potential within their colons to harbor other lesions or subsequently develop them. Certainly, it would appear that a patient with a carcinoma and associated polyps in the resected specimen has a far greater chance of developing another colic carcinoma than the person who has a carcinoma without associated polyps. Swinton and Warren [9] and Lockhart-Mummery and Dukes [10] continually preached the precancerous nature of colonic polyps. Several authors have recently expressed the same opinion. Rider and associates,[11] in 1954, found that the incidence of carcinoma in patients with polyps was five times as great as in those without polyps. Turell [12] has pointed out that, whereas the incidence of polyps in the general population is between 2 and 7%, 37 of 150 patients (24.7%) with carcinoma of the colon had associated polyps.

On the other hand, Spratt and associates [13] have shown that there may be no relation between polyps of the colon and the development of carcinoma. They make the point that the distribution of polyps is different from that of carcinomas of the colon and, further, that there is not the expected random distribution of polyps around the carcinoma; rather, lesions in the ascending colon have more polyps distal to them and those in the descending colon have more polyps proximal to them. This is not surprising, since necessarily there would be a greater segment of intestine distal to most lesions of the ascending colon and proximal to most lesions of the descending colon and rectum. Furthermore, as Lockhart-Mummery and Dukes [10] pointed out many years ago, it is quite probable that a carcinoma may cause retrogression and destruction of the benign lesions in its immediate vicinity. Turnbull [14] has also been impressed with the relative benignity of adenomatous polyps of the colon and rectum. He reviewed the histories of 54 patients followed up from 4 to 15 years who had had polyps in which carcinomatous degeneration had occurred and had been treated by local therapy, such as fulguration. In this group there were seven deaths, none due to carcinoma, and he concluded, therefore, that carcinoma in a polyp is a different disease from true colorectal carcinoma and that for this lesion local therapy is sufficient.

Lillehei and Wangensteen [7] have attempted to prevent the occurrence of metachronous carcinoma by the use of subtotal and total colectomy for lesions distal to the hepatic flexure of the colon and not involving abdominal-perineal resections. We have already mentioned some of their findings in these resected specimens. They refer to the observation made by one of us [15] during the course of subtotal colectomies for acute and chronic obstruction of the large intestine of the presence of many previously undetected polyps in other parts of the colon. In a recent review of 1,856 adenomatous lesions in 1,335 patients, Grinnell [16] discusses six different species of polypoid disease, and he points out that in 67 patients who had developed carcinoma only 1 would have been benefited by more radical surgery.

Summary and Conclusions

We believe that the only way in which the phenomenon of metachronous carcinoma can be prevented is by making an intensive effort to eradicate the source of the disease. In our opinion this can be done by performing a subtotal or total colectomy whenever polyps are noted in the resected specimen at the time of surgery. In the study reported here it was found that of 61 patients with metachronous carcinoma who had been followed up adequately, almost 50% had polyps within the original resected specimen in addition to the carcinoma, the great majority of these being located within 12 cm. of the carcinoma. This would suggest that, whenever a carcinoma of the colon is removed and true adenomatous polyps are noted in the immediate vicinity, a much more radical procedure, such as subtotal colectomy, should be performed. Whether subtotal colectomies should be performed for all carcinomas of the colon is a point still under debate, but the present study indicates a more radical approach at least in the specific instances mentioned above. It was also shown that 12% of 1,100 patients with potentially curable lesions had a second carcinoma in the colon, either simultaneously or subsequently.

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PREOPERATIVE FACTORS IN PRODUCTION OF CARDIAC ARREST

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A study was made of 30 cases in which cardiac arrest occurred during surgical anesthesia in the absence of respiratory obstruction, hemorrhage, shock, or overdosage with anesthetics. Twenty-six of the 30 occurred during general anesthesia, and 16 of the 30 involved elective operations. Half of the operations were abdominal. Two patients were resuscitated and survived without sequelae attributable to the cardiac arrest. Eight were temporarily resuscitated and survived as long as 10 days but eventually died from cerebral damage. One other patient died four days after resuscitation, probably because of circulatory abnormalities. Retrospective study showed that serious disease preexisted in all but 1 of the 30 patients and could have been recognized by more thorough preoperative tests. If full advantage is to be taken of recent advances in anesthesiology, there should be no relaxation of the care with which patients are prepared for surgery.

Cardiac arrest has become a serious problem to all persons concerned in the operative management of patients. Statistics show an apparent increase in the number of such grave occurrences. Despite an increased knowledge of cardiac physiology due to recent experimental and clinical studies, exact clarification of the etiology of onset is not known. Various factors have been implicated and all, undoubtedly, play some part. Hypoxia, hypercapnia, vagovagal reflexes, various anesthetic agents, unsuspected anoxia, and preexisting disease apparently participate. Many people blame the use of intravenously given barbiturates and muscle relaxants, others the use of too many different combinations of anesthetic gases. Anyone who has been around a surgical locker room after such a catastrophe will hear the statement that "we ought to go back to open-drop ether." The following analysis of 30 cases of cardiac arrest is presented with the realization that no statistical evidence can be derived from such a limited number. However, it should be thought-provoking and cause sober consideration of the facts presented.

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Subjects and Procedures

During the past five years there have been 33 cases at Greenville General Hospital in which effective cardiac action ceased in an anesthetized patient. Of this number, three patients were moribund at initiation, despite vigorous preoperative measures, and will not be considered. There were two cases of evisceration in gravely ill patients, and one patient had obstruction of the large intestine and peritonitis, with shock refractory to adequate preoperative blood and fluid replacement. No intracranial procedures that ended in operative death were included, since the mechanism of cardiac arrest was probably secondary to central damage. The classification of "true" cardiac arrest was given in no case in which inadvertent obstruction to airway (including regurgitation), uncontrolled intraoperative hemorrhage with prolonged shock, or overdosage of anesthesia had occurred. These, we felt, properly should be placed in the category of "operating room" or "anesthesia deaths." General inhalation or intravenous anesthesia is used in this hospital much more frequently than spinal anesthesia alone or with supplement. This leaves 30 cases worthy of consideration. All cases of true cardiac arrest were analyzed individually and the collected results tabulated.

Tabulation of Data Relevant to Thirty Cases of "True" Cardiac Arrest

	No.
Total anesthetics	68, 918
Total cardiac arrests	33
Total "true" arrests	30
General anesthesia	26
Spinal anesthesia	1
Spinal with supplement	3
Elective procedures	16
Emergency	14
Type of surgery	
Neurosurgery	3
Abdominal	15
Genitourinary	2
Thoracic	3
Head and neck	1
Orthopedic	3
EENT	3
Total patients with faulty preoperative care	14
Incorrect diagnosis	5
Failure to replace blood and/or fluid losses	12
Patients with preexisting cardiovascular disease	12
Inadequate cardiovascular evaluation and treatment	4
Arrests with massage	18
Total surviving without sequelae	2
Total surviving with sequelae	0
Patients in whom prodromata absent	4

The above data indicate that the management of the so-called cases of true cardiac arrest was not ideal in all but four. It should be pointed out that many patients were adequately evaluated and treated and accepted for surgery as a calculated risk. The greatest preventable error occurred in failure to institute proper blood, fluid, and electrolyte replacement.

Incorrect diagnoses occurred in two of the patients with traumatic injuries. In many cases this is, of course, not preventable but it emphasizes the fact that trauma is often multiple and that observation and rapid diagnostic measures such as peritoneocentesis, thoracentesis, and adequate roentgenographic examinations are of utmost importance.

Inadequate replacement of fluid and electrolytes was present in six cases, most frequently associated with patients undergoing surgical procedures of the gastrointestinal tract. This should reemphasize the marked losses of fluid which may occur from vomiting, intraluminal influx of fluids, or diarrhea which occasionally occur in the surgical patient. Blood volume studies should be obtained, when possible, from those patients in whom absolute fluid deficiencies may be present. Electrolyte studies, however valuable, are not reflective of the true status in many patients and must be judged together with the entire clinical aspect of the patient. Here, the understanding of the pathophysiological principles involved is far more valuable for the practical calculation of pertinent deficits than too heavy reliance on a laboratory value.

Failure to replace blood and/or active bleeding in nine cases was considered to be of prime importance in initiating sequelae of hypoxia. This situation occurred, however, more frequently in the patient who initially had active bleeding refractory to nonoperative measures, in which case operation was mandatory for control of hemorrhage. Again, preoperative studies of blood volume, hematocrit, and hemoglobin levels are invaluable.

With regard to blood, fluid, and electrolyte deficits there are really few emergency situations during which time cannot be taken to institute measures to restore an adequate volume of circulating blood and replace deficits. Operation should be delayed until signs of clinical improvement are manifest. The detrimental aspects of inadequate preparation are particularly impressive in the geriatric patient. The comparatively short time required for replacement of deficits more often than not pays large dividends by markedly increasing the patient's chances for survival.

Preexisting cardiovascular disease is determined by the patient's history or evidence of such disease as is manifested by hypertension and changes in the fundus, venous pressure and circulation time, and ECG changes if such were determined. No patients were presumed to have such disease merely on the basis of age or mild elevation of blood pressure. Inadequate cardiovascular evaluation and treatment consists of failure to investigate the etiology of hypertension, failure to investigate cardiac failure if signs or symptoms were present, or inadequate measures of control.

Many of the stress situations known to be associated with cardiac standstill may, at times, be tolerated quite well by the normal heart. This is not true in the diseased heart, however. Myocardial damage, chronic hypoxia (in cases of coronary atheroma or secondary to pulmonary hypoventilation), valvular disease, and prolonged "heart strain" all predispose to decreased cardiac reserve. Sudden changes in blood pressure, particularly hypotension, render the patient more vulnerable to cardiac stress.

Preexisting renal disease is determined by a finding of grossly abnormal urinalysis, history, or ancillary studies, such as determination of the blood urea nitrogen level or intravenous pyelography. One must remember the close association of such renal disease with hypertensive, cardiac, and diabetic patients. When renal disease exists, alleviation of fluid and electrolyte imbalances, administration of antibiotics, and dietary and nutritive measures combined with adequate rest and supportive therapy must be instituted as indicated.

No cases of chronic lung disease were found, but it is significant that preoperative pulmonary function tests were not recorded in the three cases of cardiac arrest occurring in patients undergoing pulmonary surgery. Pulmonary disease of many types may produce pulmonary insufficiency with hypoxia and hypercapnia by tracheobronchial obstruction, increased secretions, atelectasis, and effusions. Pulmonary function tests will often signal to the surgeon a decrease in pulmonary reserve. Spirometric measurements of timed vital capacity, maximum breathing capacity, residual lung volume, arterial oxygen saturation, pH, and arterial carbon dioxide content are all important in the assessment of pulmonary function.

Of extreme importance is the recognition of pulmonary pathology in patients undergoing surgery for conditions unrelated to the former. One has a tendency to ignore or minimize the existence of lung disease in these patients. Most patients with pulmonary disease can, to a large extent, be controlled for surgery preoperatively by the use of antibiotics if indicated, bronchodilators, postural drainage, and respiratory exercises. The extraoperative use of the positive-pressure breathing apparatus in selected patients will frequently decrease operative risk by decreasing hypoxia and hypercapnia, decreasing atelectatic areas, and lessening the amounts of secretions. Also, the elective-surgery: operative-risk relationship should be adequately and honestly evaluated individually.

In analyzing the number of cardiac arrests it was revealed that only two patients survived without any evidence of sequelae. Eight others survived as long as 10 days but eventually died from cerebral damage. One other patient survived for four days without evidence of brain damage. At autopsy, an old pulmonary artery thrombosis was found and thought to be the etiological factor in production of chronic cor pulmonale present some time prior to surgery. Cardiac arrest occurred in this patient during induction of anesthesia. Of the total number of patients in the group in whom true cardiac arrest occurred, 18 underwent cardiac massage.

Comment

Due to the fact that laboratory research of a clinical nature in this field is obviously impracticable, it is our opinion that a regular periodic review of cases of cardiac arrest should be instituted in all hospitals and that they should be presented for discussion and evaluation before the entire hospital staff. In addition, it is felt that a standard review should be formulated and channeled to a national committee when completed. The existing confusion between the terms "deaths in the operating room," "anesthesia deaths," and "cardiac arrest" may be considerably clarified. Accurate and uniform data concerning the morbidity and mortality of this serious condition can be accumulated. We wish to emphasize that this diagnosis, where clearly applicable, should be inserted into the hospital record. In this manner, many more cases would be available for detailed study and analysis. Further, adequate knowledge of the accepted methods of cardiac resuscitation should be a prerequisite for operating privileges, regardless of the specialties concerned.

Summary

This study, while limited in scope, points to the lesser importance of anesthetic factors in production of cardiac arrest, since only four such accidents occurred in healthy patients without evidence of prodromata. In all other cases, serious preexisting disease, of either an organic or a metabolic nature, was present. The poor survival rate of patients in this and other series emphasized the grave nature of such accidents. The recognition, prevention, elimination, or control of preoperative factors are important influences on the survival rate. It would appear that anesthesia and the advances made in that field, rather than being responsible for most cases of cardiac arrest, have prompted poor preparation of operative patients in the belief that today "anesthesia is safe."

2 Medical Court (Dr. Bomar).

VITAL ACTIVITY OF EXCISED CORNEA.—A rabbit cornea can be clamped in vitro between two chambers and kept alive and functioning for eight hours. Under these conditions the cornea maintains the ability to lose thickness when warmed after previous cooling; its electric resistance is of the order of several thousand ohms, virtually all due to the epithelium; and the epithelium generates an electric potential up to 40 mv, the aqueous humor side being always positive with respect to the tear fluid side.—A. Donn, M.D., D. M. Maurice, Ph.D., and N. L. Mills, B.S., *A. M. A. Archives of Ophthalmology,* November, 1959.

PROPHYLAXIS AND TREATMENT OF CARDIOVASCULAR EMERGENCIES IN INFANTS AND CHILDREN

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It is necessary to recognize certain cardiac disorders early because prophylaxis may prevent crises in which emergency treatment is required. Prophylaxis is especially important to prevent recurrence if a child has had a first attack of rheumatic fever. In children with congenital cardiac defects, medical methods of management have their place along with surgery in making sure that conditions do not suddenly worsen to the point where surgery has to be done as an emergency measure. Cardiovascular emergencies that are treated medically include congestive heart failure, arrhythmias, cerebral hypoxia, cerebrovascular accidents, bacterial endocarditis, shock syndrome, hypertensive vascular crisis, hypervolemia caused by excessive venoclysis, and digitalis intoxication. Pericardial tamponade, cardiac arrest, and certain types of congenital heart diseases, however, need to be treated surgically.

The day-to-day acute problems involving the cardiovascular system in infants and children, which confront not only the pediatric cardiologist but, more often, the pediatrician and the general practitioner, commonly terminate dramatically, either favorably or unfavorably. This requires on the part of the physician a clear-cut awareness of these emergencies and a well-integrated therapeutic approach to combat them. This article is limited to an attempt to provide a simple and concise outline of both the prophylactic and the therapeutic methods we pursue when faced by cardiovascular emergencies; it does not deal with either the diagnostic aspects or the indications, mode of action, side-reactions, or contraindications of the drugs used in these conditions.

Prophylaxis of Cardiovascular Emergencies

The undisputed importance of chemoprophylaxis in rheumatic heart disease has gained universal recognition in the last 10 years. This is probably one of the greatest strides achieved in this field in this decade. In congenital malformations of the heart the frequency of complications likewise is lessened to a significant degree by adherence to certain standards of preventive measures.

Prophylaxis in Rheumatic Fever and Rheumatic Heart Disease.—Although the exact mechanism is not known, the cause-and-effect relationship between group A beta-hemolytic streptococcic infection and rheumatic fever is well established. The first attack of rheumatic fever frequently does not lead to organic heart disease. It is recurrence of attacks, initiated each time by reinfection with this strain of hemolytic streptococcus, which eventually results in serious heart disease. These recurrences can almost always be prevented by a continuous prophylaxis against streptococcic infection. For this reason, all patients with a well-documented history of rheumatic fever, with or without evidence of heart disease, should be under this continuous prophylactic regimen during their entire pediatric age. We believe that even children who live in poor socioeconomic surroundings but with a definite family history of rheumatic fever, such as the presence of rheumatic heart disease in one or more siblings, should also be placed on this regimen.

Prophylaxis against streptococcic infections consists of administration of any one of the following medicaments: (*a*) an oral dose of 250,000 units of penicillin, twice daily, or (*b*) 7.5 to 15 grains (0.5 to 1 Gm.) of sulfadiazine tablets, daily, or (*c*) 1,200,000 units of benzathine penicillin G, given intramuscularly every three to four weeks. The few recurrences we encountered in our patients were attributable to their irregularity in taking medicaments rather than to the type of prophylaxis used. In the presence of a strongly suspected or a bacteriologically proved streptococcic infection these patients, even while under prophylaxis, should be treated with a 10-day course of either penicillin tablets, 250,000 units four times daily, or 300,000 units of procaine penicillin G given intramuscularly, every two to three days; or a single intramuscular injection of 1,200,000 units of benzathine penicillin G. Sulfonamides cannot be used for eradication of the streptococcic infection.

Prophylaxis Against Bacterial Endocarditis.—Although infrequent in the pediatric age group, the danger of contracting bacterial endocarditis is al-

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ways a possibility in children with congenital or rheumatic heart disease. Before performance of any surgical procedure such as tonsillectomy or dental extraction is attempted, a prophylactic dose is given of either penicillin tablets, 250,000 units four times daily, or 600,000 units each day of procaine penicillin G, intramuscularly, for two days prior to and two days after the operation. On the day of operation 300,000 units of benzathine penicillin G combined with 300,000 units of procaine penicillin G is given intramuscularly.

Medical Prophylaxis for Patients with Congenital Malformations of the Heart for Whom Surgery Is Not Yet Advisable or Not Yet Feasible.—With the advent of open-heart surgery and the meteoric progress in this field, a new horizon has appeared in the field of therapy for patients with congenital malformations of the heart. The successful corrective operations repeatedly demonstrated in ventricular septal defect, tetralogy of Fallot, atrial septal defect, combined mitral valvular disease, and other conditions are samples of what modern cardiovascular surgery can do. One may, however, get drowned in the swelling enthusiasm that goes with this new discovery and forget that these techniques are still accompanied by serious hazards. We do not advise open-heart surgery even for large ventricular septal defects during the first year or two of life. Our experience and studies show that while these infants have serious cardiac and respiratory difficulties during infancy, they improve considerably both symptomatically and objectively after the 1st or 2nd year of life. The high percentage of morbidity accompanying corrective surgery at this age makes us feel that medical treatment alone during infancy, with the purpose of postponing surgery to a safer age, would result in a lesser mortality than if surgery were done right away, irrespective of the severity of the ventricular septal defect. The proper use of antibiotics for repeated respiratory infections and of digitalis for heart failure are better therapeutic tools during this period of life. These statements apply also to other congenital cardiac anomalies for which open-heart surgery is indicated.

Patients with cyanotic forms of congenital heart disease are prone to develop serious complications from polycythemia or from anemia. The common denominator appears to be the cerebral hypoxia that results from either of these two conditions often manifested by the typical hypoxic spells frequently noted in tetralogy of Fallot. In the presence of polycythemia special care should be exerted to avoid any dehydration. Intake of fluids should be encouraged freely, particularly during hot weather, and any fluid loss from diarrhea or vomiting should be properly replaced. On rare occasions, when the hematocrit is in the range of over 75%, venesection may be advisable, especially in the presence of these symptoms. Oral administration of iron is indicated in patients with hypochromic anemia, even if the red blood cell count is only slightly reduced, because in these cyanotic patients such a red blood cell count is evidence of severe anemia.

Surgical Prophylaxis in Patients with Congenital Malformations of the Heart.—Cardiac surgery may be considered a prophylactic measure when done in those children who are potential candidates for serious cardiac complications in later life, although at present they are relatively asymptomatic. All patients with patent ductus arteriosus who are doing well are advised to have surgery after the 3rd year of life. Those with coarctation of the aorta should undergo surgery when they are about 7 to 9 years old. Patients with atrial septal defects of either primum or secundum types who are fairly asymptomatic should undergo open-heart surgery by about their 5th to 7th year of age. Valvulotomy in patients with isolated pulmonary stenosis is advised at about the same age range, but only when the right ventricular pressures are over 80 to 100 mm. Hg. We do not advise any form of palliative shunt operation or valvulotomy on patients with cyanotic types of congenital malformations of the heart with insufficient pulmonary blood flow if they are doing well and are free from hypoxic spells.

Treatment of Cardiovascular Emergencies

Medical Emergencies.—Cardiovascular emergencies which can be treated medically fall into nine major groups.

Congestive Heart Failure: Rest and comfort are mutually related and essential for the proper management of heart failure. Not uncommonly certain procedures, like nasal oxygen inhalation or forcing or tying patients to a semirecumbent position, do more harm than good because of the apprehension and excitement they provoke. The best rest can be accomplished only with the best comfort. If necessary, phenobarbital and/or codeine should be given to attain this end. An oxygen tent running at 8 to 10 liters of oxygen per minute is indicated in the severe cases. Toilet privileges should be allowed as soon as possible. A good dictum to remember is "Do unto others as you would have others do unto you." A low-salt diet is prescribed, and infants with refractory edema should be given Lonalac, a powdered milk preparation with a low sodium content (1 fl. oz. of the prepared milk has 0.75 mg. of sodium as compared to 1 fl. oz. of cow's milk, which contains 16.5 mg. of sodium). Fluid intake need not be restricted to less than what these children normally require. The digitalis preparation of choice for any particular case is the one the physician is best acquainted with. We believe that any digitalis preparation given in an appropriate dosage is just as good as any other. We routinely use digitoxin (Digitaline Nativelle). This is dispensed in a 50% alcoholic solution of which one minim contains 0.02 mg. of digitoxin. The initial digitalizing dose depends on age and weight and usually consists of 0.03 mg. per pound of body weight in infants, 0.02 mg. per pound of body weight in children aged 1 to 3 years, and 0.01 mg. per pound of body weight in children over 3 years old. One-half of the total calculated digitalizing dose is given initially and the other half is divided into two doses and given at six-or-eight-hour intervals. The daily maintenance dose is roughly one-tenth of the digitalizing dose. Our clinical experience with acetyldigitoxin (Acylanid) in children has been just as good as with digitoxin, with the same dosage schedule. We have not used powdered digitalis leaf or its tincture. For rapid digitalization lanatoside C (Cedilanid) may be given intravenously, in a similar dose as above. This is followed by a slow and cautious redigitalization 24 to 36 hours later, with use of digitoxin or acetyldigitoxin. The use of mercurial diuretics is indicated in the presence of moderate to marked edema. Either meralluride (Mercuhydrin) sodium or mercaptomerin (Thiomerin) sodium are given in initially small doses of 0.1 to 0.2 cc. intramuscularly and are increased by small increments every two or three days, until the desired effect is obtained. These diuretics are usually given two or three times a week. Patients manifesting mercurial fastness may be given aminophylline, in a dose of 6 mg. per kilogram of body weight intramuscularly one hour after the mercurial injection, or 1 to 3 Gm. of ammonium chloride orally, in three divided doses daily for two days prior to the mercurial injection. This may be repeated every week. Acetazolamide (Diamox), a carbonic anhydrase–inhibitor, may also be added to these diuretics, in a daily oral dose of 5 mg. per kilogram of body weight in divided doses for two to three days prior to the mercurial injection. Chlorothiazide (Diuril) has also been reported to be satisfactory in a dose of 125 to 250 mg. given orally twice daily, with supplements of 1 Gm. of potassium chloride daily. Our experience with this drug is limited. One of the dangers to be guarded against during or after the induction of diuresis in infants and young children is the incidence of electrolyte disturbances. The low-sodium syndrome (hyponatremic acidosis), low-chloride syndrome (hypochloremic alkalosis), high-chloride syndrome (hyperchloremic acidosis), hypopotassemia, and hyperpotassemia are infrequent side-effects but, if present, can be more treacherous than the heart failure itself. A constant awareness of these possibilities, the judicious use of digitalis, mercurial diuretics, and ammonium chloride, as well as proper electrocardiographic control, all help to avert this complication. In acute rheumatic carditis and in carditis of other collagen diseases steroids should be given early, in sufficient amounts, and for a sufficiently long period, usually from 8 to 12 weeks. If rheumatic activity persists, steroids may be given for a longer period. Up to 300 or 400 mg. daily of cortisone acetate, or its equivalent (one-fifth of this amount) in prednisone (Meticorten), is given daily for about three weeks and then gradually decreased by about 25 mg. at weekly intervals. Administration of supplementary potassium chloride, 1-2 Gm. daily, and a low-sodium diet are essential in steroid therapy. When congestive heart failure is accompanied by severe anemia, packed red blood cell transfusion, given very slowly and in small quantities of no more than 3 to 5 cc. per pound of body weight, is indicated. This may be repeated each day for several days as required, but no effort to correct the anemia completely with one or two transfusions should be attempted.

Arrhythmias: It is gratifying that most of the alarming and potentially dangerous disorders of the pacemaking activity of the heart can be diagnosed and successfully treated. The present-day mainstays in the antiarrhythmic management of these disorders consist of reflex vagal stimulation and administration of rapidly acting digitalis, quinidine, and procainamide hydrochloride. The three types of arrhythmia which can be classified as cardiovascular emergencies are as follows:

First is paroxysmal supraventricular tachycardia, which needs to be carefully distinguished from other tachycardias. Sinus tachycardia, or even the normal tachycardia in infancy, may sometimes be mistaken for paroxysmal tachycardia. One should be aware of the normal differences in the heart rate of the different age groups to avert this blunder and avoid scrupulously the chance of introducing an unwarranted anxiety on the part of the parents over a harmless situation. For example, a heart rate of 160 to 170 per minute in an infant may be normal.

Reflex vagal stimulation should always be tried first. The right carotid sinus is compressed for about one minute, while the examiner listens with the stethoscope at the same time. If this fails, the left side is tried. Once the rhythm changes, the pressure is released immediately. The procedures hitherto advocated, such as pressure on the eyeball or the induction of vomiting, are not usually indicated. Digitalis is the drug of choice. A rapidly acting digitalis preparation like lanatoside C or the ordinary, slow-acting glycoside may be used, depending on the severity of the condition. The dosage has been previously discussed. Not uncommonly, these attacks are precipitated by severe infections such as pneumonia or empyema, and the use of antibiotics would then be a necessary supplement to the therapy.

We have administered acetylcholine bromide intravenously in our critically ill patients, with good results. Its pharmacological antidote, atropine sulfate in a dose of 1/500 grain (0.12 mg.) should always be on hand in case cardiac standstill develops. Since acetylcholine bromide is destroyed rapidly in vivo, its effect is instantaneous, and the dose can be repeated every three to five minutes without any danger of cumulative effect. We usually start with a dose of 2 mg. and increase it by 2 to 4 mg. every three to five minutes, until conversion is attained. Continuous monitoring by an electrocardiograph is essential for this procedure. We have no experience with the use of systemic arterioconstrictor drugs such as methoxamine (Vasoxyl) hydrochloride, phenylephrine (Neo-Synephrine) hydrochloride, or levarterenol (Levophed) bitartrate in this condition in children.

Second, atrial flutter and atrial fibrillation are rarer types of supraventricular arrhythmia. Digitalis is again the drug of choice. If the abnormal rhythm persists even after full digitalization, then quinidine is added to the maintenance dose of digitalis. Quinidine sulfate should be administered cautiously. Electrocardiograms both before and during the drug intake should be routinely made. After a test dose of 25 mg., 100 mg. of quinidine is given orally every two hours for as many as six doses. If no conversion occurs, this is increased to 200 mg. every two hours on the next day, again for six doses. This may still be gradually increased until the tachycardia disappears or the findings of quinidine toxicity, such as vomiting and abnormal widening of the QRS complex to more than 30% of the control tracing, appear in the electrocardiogram. If the medicament cannot be taken or tolerated orally, it may be given intramuscularly with an optimum dosage of 3 mg. per pound of body weight every two to three hours. It should be stressed that administration of quinidine should not be started before digitalization because of the danger of provoking a rapid ventricular response. A rare entity closely simulating atrial flutter is paroxysmal atrial tachycardia with block. These two conditions should be differentiated by means of an electrocardiogram because, while in the former the drug of choice is digitalis, in the latter the drug of choice is potassium chloride, since paroxysmal atrial tachycardia with block is, in most instances, due to digitalis intoxication.

Third, paroxysmal ventricular tachycardia, another type of arrhythmia amenable to medical emergency treatment, is fortunately rare in infants and children. Most of the cases are due to digitalis intoxication. The objective of therapy is to avert the inherent tendency of this type of tachycardia to progress to ventricular flutter and fibrillation. When paroxysmal ventricular tachycardia is due to digitoxicity, cessation of digitalis treatment and intravenous injection of potassium chloride is imperative. If there is no response to the latter measure, or if the condition is not due to digitalis intoxication, procainamide hydrochloride should be given intravenously and should always be accompanied by a continuous [illegible] tracing and frequent recording [illegible] ssure. A dose of 10 mg. every two to three minutes is given until the occurrence of either conversion of the arrhythmia or the appearance of either one of the two commonest side-effects, i. e., premature ventricular contractions or hypotension. A total dose of no more than 500 mg. should be given intravenously at a time. As a last resort quinidine may be given intravenously. Five cubic centimeters of quinidine gluconate (0.08 Gm. per cubic centimeter) is added to 50 cc. of a 5% glucose solution and given at a rate of about 1 to 2 cc. per minute, under electrocardiographic control. This procedure may be repeated if conversion fails to appear.

Cerebral Hypoxia: The symptom complex comprising the so-called hypoxic spells in congenital heart disease may be encountered in both cyanotic and noncyanotic patients. In the former group, its incidence is highest in severe instances of tetralogy of Fallot. During the attack, these patients should be put in a knee-chest position and given oxygen. Morphine sulfate given hypodermically, in a dose of 1 mg. for every 10 lb. of body weight, gives dramatic relief in almost all instances. The increasing frequency of these attacks carries a bad prognostic value and is a strong indication for a shunt operation. In the noncyanotic group these spells occasionally may be noted in moderately severe or severe aortic valvular or subvalvular stenosis. Such patients should be digitalized and their activity restricted. Just as in tetralogy of Fallot, the presence of these spells strongly indicates the severity of the obstruction to blood flow and therefore the need for early surgery.

Cerebrovascular Accidents: Cerebral thrombosis or embolism may occur in patients with cyanotic congenital malformations of the heart associated with polycythemia. An important contributing, and probably precipitating, factor in the majority of instances is dehydration. Prompt therapy is required which fortunately is the same in either condition. Venesection may be done, the amount of blood removed depending on the patient's age, weight, and red blood cell count. Removal of about 5 cc. of blood per kilogram of body weight is relatively safe. A continuous intravenous infusion for 12 to 24 hours of 5% dextrose in water or saline is given after the venesection. Anticoagulant therapy is instituted with heparin sodium, 0.5 mg. per kilogram of body weight, given intravenously every hour. The aim of this treatment is to maintain a prolonged coagulation time of 20 to 30 minutes for a period of at least 24 hours. If a septic course accompanies the neurological picture, the possibility of a brain abscess should be seriously entertained, and diagnostic and therapeutic measures, including surgery, should be directed toward that end.

Bacterial Endocarditis: Every effort to determine the offending organism and its drug sensitivity should be made, but with the least jeopardy to the patient in terms of postponing the initiation of therapy. We routinely take three to six blood cultures daily for two days and start treatment with the assumption that the organism is penicillin-sensitive (sensitive to 0.1 unit per cubic centimeter). If the culture reveals a penicillin-sensitive organism, a four-week course of a combined dose of 1,200,000 units of aqueous and procaine penicillin G, administered intramuscularly twice daily, is given. If there is no definite improvement in three to five days, the patient is treated as if the harbored organism were penicillin-resistant. In this instance, 10 to 20 million units of aqueous penicillin is given intravenously daily, through a continuous drip infusion, for about six weeks. Streptomycin and dihydrostreptomycin are also given alternately each day, in a dose of 0.25 to 0.50 mg. twice daily. In patients who are allergic to penicillin or in cases where the organism is resistant to penicillin but sensitive to other antimicrobial drugs, the specific broad-spectrum antibiotics to which the organism is sensitive are used in high dosages (40 to 80 mg. per pound of body weight). If the organism is not known and the patient is allergic to penicillin, a four-week course of therapy with erythromycin, 40 to 60 mg. per pound of body weight in four divided doses daily, and chloramphenicol, 60 to 80 mg. per pound of body weight in four divided doses daily, is instituted.

Shock Syndrome: Sudden circulatory failure may be due to cardiac or extracardiac causes. The extracardiac causes are many and will not be discussed in detail. The common ones are trauma, acute hemorrhage, extensive burns, severe diarrhea or vomiting, intoxications, and the crisis associated with the adrenal dysfunction seen in cases of pseudohermaphroditism, adrenogenital syndrome, or in the Waterhouse-Friderichsen syndrome. The general measures in all of these conditions are aimed at the immediate restoration of the blood volume and maintenance of a satisfactory blood pressure. Whole blood plasma, or plasma-volume expanders like dextran, polyvinylpyrrolidone (P. V. P.), or even 5% dextrose in saline solution may be used for restoring the blood volume. Vasopressor drugs like levarterenol bitartrate in a dose of 4 cc. of a 1:1,000 solution should be added to any of the above infusions used and the rate of flow adjusted according to the response in the blood pressure. Oxygen inhalation is helpful. The other therapeutic measures vary, depending on the etiology of the shock. The cardiac causes for the shock syndrome are pericardial tamponade and cardiac arrest. These will be discussed later.

Hypertensive Vascular Crisis: The majority of these cases are due to acute glomerulonephritis. Not uncommonly, it is accompanied by neurological findings of the so-called hypertensive encephalopathy. Cardiac treatment in these conditions is indicated only if the blood pressure is over 140 mm. Hg systolic and over 95 mm. Hg diastolic. Magnesium sulfate is given intramuscularly, with use of a 50% solution and a dose of 0.1 cc. per kilogram of body weight. This may be repeated every four to six hours. It may also be given intravenously, with use of a 3% solution and a dose of 0.1 cc. per pound of body weight, but no more than 75 mg. per hour should be given. The blood pressure should be constantly watched during the intravenous infusion. Any toxic effect of magnesium, such as respiratory depression, should be counteracted by giving 5 to 10 cc. of 10% calcium gluconate (or chloride) intravenously. If the hypertension persists, reserpine (Serpasil) is given in a dose of 0.1 to 0.25 mg. intramuscularly, twice daily. If this is still ineffective, hydralazine (Apresoline) hydrochloride is given intramuscularly in a dose of 0.2 to 0.25 mg. per kilogram of body weight every four to six hours. In the presence of congestive heart failure, digitalis should be given. Usually this is needed only for a very transient period of about one week.

Circulatory Overloading in Transfusions with Blood or Other Fluids: Most of the cases we have seen were in infants and young children who had had blood transfusions. The direct cause appears to be either an excessive volume of blood or fluid given, or a rapid rate of infusion, or both. The overloading usually occurs in the presence of an organic heart disease The occurrence of paroxysms of dry cough during the transfusion is usually the earliest sign preceding the cervical venous engorgement, dyspnea, cyanosis, and pulmonary edema. After diagnosis, the transfusion should be stopped immediately and the venous pressure reduced by the application of tourniquets on the extremities or preferably by phlebotomy. When pulmonary edema is present, morphine sulfate, in a dosage of two-thirds of the calculated dose of 0.1 mg. per pound of body weight, combined with 1/400 to 1/600 grain (0.15 to 0.12 mg.) of atropine sulfate are given hypodermically, and the routine treatment for acute congestive heart failure is initiated.

Digitalis Intoxication: Anorexia and vomiting are common general manifestations of digitalis intoxication. Usually, toxicity is heralded clinically by the presence of extrasystoles, tachycardia, or heart block. The frequent electrocardiographic findings consist of an incomplete atrioventricular block or dissociation, various forms of supraventricular arrhythmias, or premature ventricular contractions. If untreated, paroxysmal atrial tachycardia with block, ventricular tachycardia, and even ventricular fibrillation and death may ensue. Treatment requires discontinuance for several days of administration of digitalis and diuretics and a careful observation of the patient, with much reliance on frequent electrocardiographic tracings. Potassium chloride is given orally in a dose of 100 mg. per kilogram of body weight per day, in divided doses. In the presence of a more serious arrhythmia this may be given by intravenous drip infusion, with use of a concentration of 20 mEq. of potassium chloride in 500 cc. of 5% dextrose in water (1.5 Gm. of potassium chloride in a 500-cc. solution), but always accompanied by a continuous monitoring electrocardiogram.

Surgical Emergencies.—There are three cardiac emergencies which require treatment with a variety of surgical procedures.

Pericardial Tamponade: The vast majority of pericardial effusions resolve spontaneously and it is very probable that a large number of these cases remain undiagnosed. In the presence of rapidly accumulating fluid symptoms develop swiftly, and the picture of cardiac tamponade appears. The most common cause for tamponade in children is purulent pericarditis. Pericardiocentesis dramatically changes the clinical picture. Our usual approach in children is to introduce the needle in the left costoxiphoid space close to the sternum. Once a purulent pericarditis is diagnosed, pericardiostomy should be done to promote complete drainage, and aqueous penicillin should be instilled locally, inside the pericardial sac. Antibiotics are given as well to control the original infection.

Cardiac Arrest: Cardiac arrest may be due to cardiac standstill or, less commonly, to ventricular fibrillation. This treacherous incident respects no age and has no preference for normal or abnormal hearts. It occurs mostly during surgery and during the induction of anesthesia. However, mechanical stimulation of the mucosa of the gastrointestinal, respiratory, or genitourinary tracts can also precipitate the vagovagal reflex leading to this condition. Immediate action is the most decisive factor responsible for the success or failure of the management of cardiac arrest. If the patient is to survive at all, and certainly without brain injury, an effective circulation and a patent and functioning respiratory system must be established within three or four minutes. Once the diagnosis is suspected, tracheal intubation is done and the lungs inflated and deflated with 100% oxygen. In the absence of the necessary equipment, mouth-to-mouth artificial respiration should be immediately started and continued until intubation can be done. Meanwhile, the chest is opened along the fourth left interspace without respect for asepsis, and cardiac massage is started. The radial or femoral pulses should be palpated to check if the massage is mechanically effective. The rhythmic massage should be maintained at a rate of 70 to 80 per minute, with a vigorous compression, a rapid relaxation, and a short pause to promote filling of the heart chambers. If the heart remains flaccid, 1 cc. of levarterenol bitartrate in a 1:1,000 solution, diluted to 5 cc. with saline solution, is injected intracardially. Five cubic centimeters of 10% calcium chloride or 1 cc. of a 1:10,000 solution of epinephrine may also be given similarly. When ventricular fibrillation is present or sets in, an electric defibrillator is used. It should be stressed that defibrillation is useless in the presence of a flaccid myocardium. If the heart remains in this condition, manual massage should be continued and levarterenol bitartrate injected intracardially until the myocardium regains tone and appears pink. When this is attained, the heart is ideally receptive for the electric shocks from the defibrillator. This should be repeated at intervals until a cardiac pacemaker takes over and restores an effective circulation.

Emergency Cardiac Surgery: There are certain congenital heart diseases which, on account of the severity of their malformations, are a threat to life unless emergency cardiac surgery is done. Surgery, palliative or corrective, is definitely indicated at any age in the following conditions: (1) severe cases of patent ductus arteriosus and atrial septal defects with left-to-right shunt; (2) severe cases of isolated pulmonary stenosis; (3) double aortic arch with dysphagia and repeated respiratory infections; (4) severe coarctation of the aorta and severe aortic stenosis which do not respond to adequate medical management; (5) complete transposition of the great vessels; (6) severe cases of tetralogy of Fallot, tricuspid atresia, single ventricle with severe pulmonary stenosis, and severe pulmonary stenosis with a right-to-left shunt at the atrial level; and (7) anomalous entrance of all pulmonary veins into the supracardiac vessels. Except in the very rare cases where it is accompanied by inactive, severe mitral stenosis, surgery is not indicated in rheumatic heart disease in children.

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AMERICANS BORN ABROAD.—This past year, more than 800,000 of our citizens traveled abroad. Each traveler had to prove his birth facts to obtain a passport. These travelers, together with our military personnel stationed in foreign countries, reported nearly 50,000 births to U. S. consular officers throughout the world. Providing satisfactory birth-record service for children born abroad who are U. S. citizens is a problem second only to that of obtaining birth certificates for the increasing number of alien children being adopted in the United States.—H. V. Aune, The Importance of Vital Records in Today's Society, *Public Health Reports*, November, 1959.

PLATELET TRANSFUSION WITH USE OF BLOOD IN PLASTIC BAGS FROM ROUTINE STORAGE

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The hemorrhagic manifestations of thrombocytopenia can be effectively controlled by the infusion of human platelets[1] but the hemostatic effect is relatively transient. Despite this limitation, platelet transfusion can be used to prepare the thrombocytopenic patient for emergency surgery and to control thrombocytopenic bleeding which occurs prior to, or in spite of, adequate "steroid" therapy. These emergencies require immediate treatment, but the usual methods for the preparation of platelet concentrates, platelet-rich plasma, or platelet-enriched whole blood incorporate techniques which are not available to the usual hospital blood bank, i. e., low-temperature processing, special anticoagulants, and the immediate availability of compatible blood donors. The inference that these latter techniques are essential to obtain viable platelets has deprived many hospitals of a valuable therapeutic tool. McGovern[2] has shown that low-temperature processing and special anticoagulants are not essential, but his method necessitates the immediate availability of compatible blood donors. It is our contention that platelet transfusion, when indicated, is an emergency procedure which can be made readily available if "bank blood," which has been collected in containers with nonwettable surfaces, is used.

Results of Platelet Transfusion in Secondary Thrombocytopenia

No. of Case	Platelet Counts, × 10³				Bleeding Time, Min.				Clot Retraction, %				Prothrombin Consumption, Sec.					Clinical Observations	
	Preinfusion	Maximum	Hr. Postinfusion	96 Hr. Postinfusion	Preinfusion	Nadir	Hr. Postinfusion	96 Hr. Postinfusion	Preinfusion	Maximum	Hr. Postinfusion	96 Hr. Postinfusion	Preinfusion	Maximum	Hr. Postinfusion	96 Hr. Postinfusion	Laboratory Results, General	Pre-infusion Hemorrhage	Post-infusion Hemostasis
Marrow Hypoplasia																			
1	26	336	2	150	+10	6	2	9	0-25	100	2	25-50	28	47	2	35	Good	Moderate	Partial
2	36	232	24	60	29	14	24	17	0-25	100	24	25	12	15	24	11	Good	Severe	Partial
	25	238	24	45	+25	15	2	15	0-25	100	2	25	13	16	2	13	Fair	None	...
3	1.2	83	2	12.5	+15	6	2	6	0	100	2	0	12	22	4	12	Good	Severe	Complete
	16	78	2	25	+15	5	4	6	0	100	2	0	11	28	4	10	Good	Severe	Complete
4	77	96	6	...	+15	5	6	...	0	50	6	...	12	18	4	...	Fair	Severe	Partial
5	63	89	4	70	+15	9	4	10	0	100	4	25	9	17	2	7	Fair	Severe	Partial
Lymphosarcoma																			
6	19	27	4	...	+15	9	4	...	0-25	0.25	6	...	16	25	2	...	Poor	Moderate	Partial
7	62	87	2	...	+15	12	2	...	0	50	2	...	13	15	2	...	Poor	Severe	None
8	36	63	24	63	9	7	4	7	0	100	4	75	14	15	2	10	Fair	Severe	None
9	64	117	2	67	+15	5	2	9	0	50	4	0	15	19	2	10	Fair	Moderate	Complete
Acute Leukemia																			
10	40	640	4	120	+20	7	4	10	25	100	4	25	18	32	4	20	Good	Severe	Complete
11	77	83	2	44	+30	15	2	15	25	50	2	25	13	16	2	13	Poor	Severe	None
Chronic Leukemia																			
12	96	237	4	53	+15	5	4	8	0	100	4	25	10	39	2	11	Good	None	...
Metastatic Carcinoma																			
13	5.7	63	4	8.7	+15	8	4	+15	0	100	4	25	15	18	2	12	Fair	Severe	Partial

Materials and Methods

Since idiopathic thrombocytopenic purpura is believed to be an autoimmune phenomenon, we excluded persons with this condition from our study and included only cases of secondary thrombocytopenic purpura. The secondary thrombocytopenia, in the cases selected, was the result of a variety of conditions, such as lymphosarcoma involving marrow, acute leukemia, chronic leukemia, metastatic carcinoma to marrow, and hypoplasia of marrow. Since 2 of the 13 patients studied were given infusions of platelets on two separate occasions, a total of 15 platelet transfusions were given to 13 thrombocytopenic patients.

Four plastic-bag units of whole blood from normal donors, compatible with the recipient and in storage less than 48 hours, were selected for processing. Anticoagulant acid citrate dextrose solution (approved National Institutes of Health formula

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From the departments of medical education and hematology of the Hektoen Institute for Medical Research of the Cook County Hospital and the Departments of Medicine of the Stritch School of Medicine, Loyola University (Dr. Tobin) and Chicago Medical School (Dr. Friedman).

A: 0.8 Gm. of acid citrate, 2.45 Gm. of dextrose, and 2.2 Gm. of trisodium citrate per each 100 ml. of water) was used to preserve the blood. The four plastic-bag units were centrifuged in a model BP international centrifuge at 1,200 rpm for 15 minutes, at room temperature. After centrifugation, the platelet-rich supernatant plasmas were transferred by a positive-pressure press into four smaller plastic bags (transfer packs). The plastic tubing, connecting each plastic-bag unit to its transfer pack, was then clamped, and the connected packs were recentrifuged in an individual cup at 2,000 rpm for 45 minutes. After centrifugation, there was a thick, whitish residue (platelets) in the bottom of each transfer pack. The clamp between each pair of packs was removed, and the supernatant platelet-free plasmas in the transfer packs were pressed back into the original blood packs, with the exception of approximately 15 ml. which was allowed to remain for the resuspension of the platelet residue. The plastic tubing connecting each pair of packs was then tied and severed. The four transfer packs were connected in tandem by plasma transfer sets, and all of the platelets were pressed into a single pack. If whole blood was desired, all of the material was pressed into a single blood pack. The platelet concentrate, platelet-rich plasma, or platelet-enriched whole blood was infused through a "platelet-recipient set" and a hemorepellent needle.

The effects of platelet transfusion were evaluated by clinical observation and serial determinations of indirect platelet count,[3] (normal: 200-400 × 10^3), bleeding time[4] (normal: one to four minutes), clot retraction[5] (normal: 100% in one to two hours), and prothrombin consumption[6] (normal: greater than 16 seconds in one hour). The results of the Rumple-Leede test were not considered reliable enough to warrant recording because of variability in interpretation, previous venipunctures, and ecchymosis.

Results

The clinical observations and laboratory data are summarized in the table. Figures 1 and 2 illustrate in detail the serial laboratory determinations used to evaluate the effectiveness of these platelet infusions.

Hemorrhagic manifestations were present in all but two of the patients prior to platelet transfusion. The bleeding was dramatically controlled in five, partially controlled in five, and poorly controlled in three patients. These clinical observations correlated well with the laboratory data. Subsequent to the 15 platelet transfusions, the platelet count increased in excess of 60,000 per cubic millimeter in 8 patients (53%), the bleeding time decreased to near normal levels in 8 patients (53%), the uniformly abnormal clot retraction became "complete" in 10 patients (66%), and the increment in prothrombin consumption was in excess of 10 seconds in 6 patients (40%).

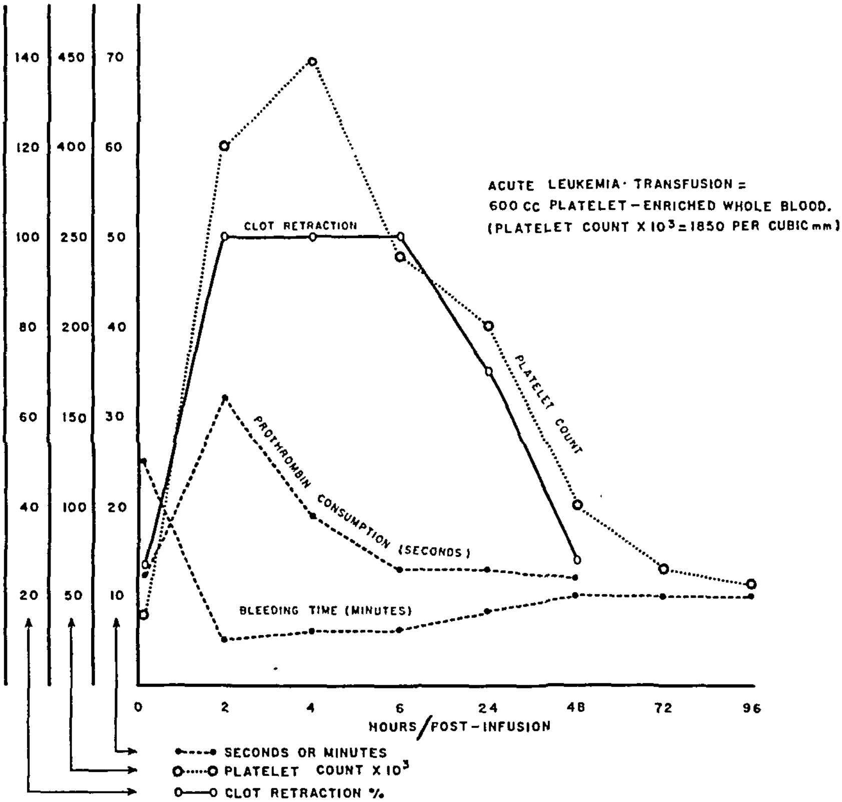

Fig. 1.—Serial laboratory determinations illustrating effects of platelet transfusion in thrombocytopenia associated with acute leukemia.

Summary

The administration of human platelets, prepared from acid-citrate-dextrose (A. C. D.)-blood in routine storage, controls bleeding in thrombocytopenic patients. We agree with McGovern[2] that the degree of control and the length of the hemorrhage-free interval depends on the etiology of the thrombocytopenia. In acute leukemia, lymphosarcoma involving marrow, plasma cell-myeloma, and metastatic carcinoma to marrow the degree of control and the hemorrhage-free interval are usually shorter than in hypoplasia of marrow. The hemostatic effects of platelet transfusion appear promptly after infusion

and invariably persist after the platelet count, bleeding time, clot retraction time, and prothrombin consumption have reverted to their abnormal pre-infusion values.

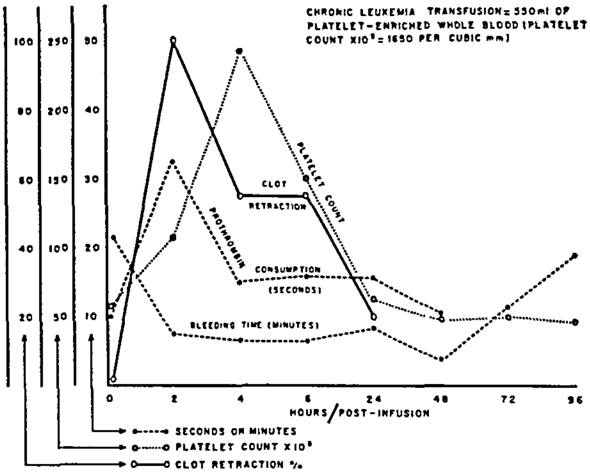

Fig. 2.—Serial laboratory determinations illustrating effects of platelet transfusion in thrombocytopenia associated with chronic leukemia.

The demonstration that human platelets can be prepared and infused without special procedures or immediately available compatible blood donors should make this therapeutic measure available to most hospitals.

Cook County Hospital, 1825 W. Harrison St. (Dr. Tobin).

This study was aided in part by a grant from the Benjamin Fishbain Fund. The authors are indebted to Mr. Thomas Scanlon of the Chicago Medical School for photography and preparation of charts.

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THE COFFEE BREAK.—With the increased demands for manpower and production during World War II, there appeared the midmorning and midafternoon cessation from work, termed in most work situations, the coffee-break. The entity of the coffee-break has entered into the conversational currency of advertising, the cartoon, the news item, and the news photograph as a recognized activity of worker, housewife and student. Introduced initially to combat work fatigue, the rest period has provided an interval for food and beverage consumption, which activity through elevation of blood level has been credited for minimizing accidents and injuries, increasing production and counteracting the nutritional deficit displayed by those who omit breakfast. In four large surveys, involving over 3,000 companies, it was seen that 70% to 90% of the organizations grant time for coffee breaks, in the belief, mostly documented, that morale, production and efficiency improved, and that fatigue, absenteeism, accident rate, turnover and waste are lowered. Dimensionally, the coffee break assumes these measurements: 35 million workers utilize rest periods as coffee breaks; 8 billion cups of coffee are consumed annually during coffee breaks (7.4% of all coffee drunk in the United States; 15% of all coffee consumed by the homemaker is drunk at midmorning and midafternoon; and rest periods represent a fringe benefit cost to the employer of 5.5¢ per employee per hour). . . . The question of the recognition of rest periods as legitimate time components of the work day has been tested in the courts, and the concept of the break has entered into collective bargaining agreements.—J. S. Felton, M.D., The Coffee Break, *Industrial Medicine and Surgery,* October, 1959.

CLINICAL NOTES

INFERTILITY DUE TO FAULTY INTROMISSION SUCCESSFULLY TREATED BY PROSTHETIC DEVICE

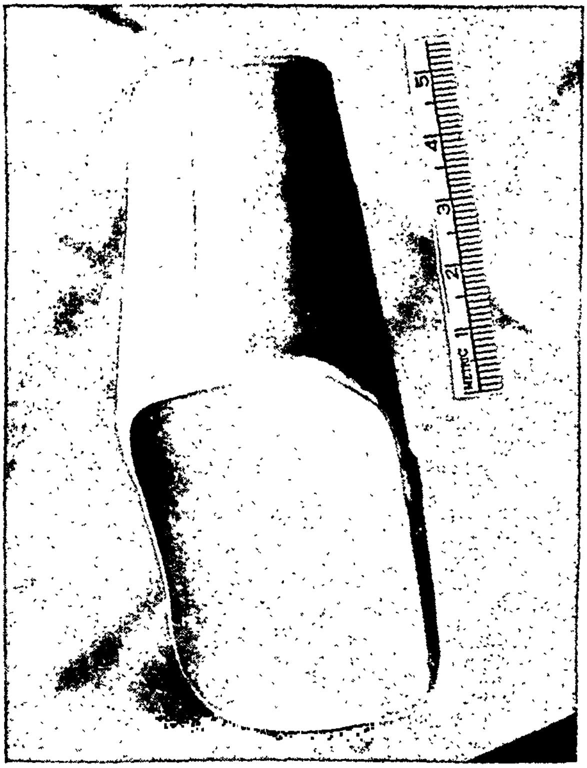
Pendleton Tompkins, M.D., San Francisco

An occasional couple is infertile because intromission of the penis in the vagina has never occurred. Intromission is imperfect if the introitus is abnormally tight or if the erection is weak. An incomplete erection in young men is nearly always psychogenic. Treatment by psychiatrists or urologists does not usually lead to improvement in cervical or vaginal insemination. In such cases of infertility there has been no alternative to artificial insemination, with use of the husband's semen. Since this entails masturbation or the equivalent to secure the specimen it is psychologically undesirable, because the fact of impotence is emphasized. Indeed, some men are unable, after a few trials, to produce an ejaculation. Thus a bad situation has been made worse.

During the past six months I have prescribed a prosthetic device for eight husbands who were seldom or never able to effect intromission. The device has been helpful in the following ways. 1. Vaginal insemination has been achieved. 2. Stronger erections are reported. 3. The husbands' confidence has been increased. 4. Wives who had never experienced orgasm during marriage have done so. 5. One wife conceived.

The eight couples employed the device for 20 months in all (one couple each for six, four, and three months, three couples for two months, one couple for one month, and one couple who found the device of no help). The one failure occurred in a patient who had been married for four years. She had a dense, narrow hymen and vaginismus and had never experienced orgasm. Intromission was not possible with or without the prosthesis until after surgical correction of the tight introitus. When relations were attempted after surgery the prosthesis was employed a few times and thereafter was not needed. This "failure" can hardly be called a failure of the device, since it was really a failure of judgment on my part to prescribe a prosthesis when it was nearly certain that surgery would be required. Six wives have not conceived but vaginal insemination is occurring. One patient, married three years before hymenotomy and one year after hymenotomy without intromission, conceived three months after her husband began using the prosthesis.

The device, called the Eros, is shown in the figure. It is a rubber sleeve of the proper size and consistency with an apron in front. When the patient wearing it is in the prone position, the weight of the gonads on the apron elevates the penis and the constricting sleeve produces engorgement. Neither wives nor husbands have reported discomfort or complications.



Prosthetic device for use in treating infertility.

No apology is made for the small number of cases; chronic failure of intromission is not a frequent problem in my practice.

450 Sutter St. (8).

Assistant Clinical Professor of Obstetrics and Gynecology, Stanford University School of Medicine.

The Eros was supplied by the DEG Corporation, San Francisco.

SEVERE CHLORPROPAMIDE TOXICITY

Edwin L. Rothfeld, M.D., Jerrold Goldman, M.D., Harold H. Goldberg, M.D.
and
Samuel Einhorn, M.D., Newark, N. J.

Chlorpropamide (Diabinese) is a potent, orally used, hypoglycemic sulfonylurea derivative that recently has been used in the management of diabetes mellitus. Earlier reports [1] of clinical trials have, in general, mentioned only minimal side-effects or none at all when the drug is used in recommended therapeutic doses.

Probably the most common complaints have been referable to hypoglycemia and consist of weakness, giddiness, and paresthesias.[2] Minor gastrointestinal symptoms have also been reported.[3] Observed hematological changes include thrombocytopenia,[4] granulocytopenia,[5] erythrocytic stippling,[2a] and eosinophilia.[6] Various skin lesions have been described, including maculopapular eruptions,[7] urticaria,[8] exfoliative dermatitis,[9] erythema multiforme,[2a] and purpura.[4] Obstructive jaundice has been mentioned in isolated reports.[10] Liver biopsy specimens in these cases have been characterized mainly by cholestasis.[11] Other less commonly noted toxic effects have been crystalluria,[2a] muscular weakness,[2b] decrease in thyroid function,[2c] and a peculiar intolerance to ingestion of alcohol.[12]

The purpose of this report is to describe a case of severe chlorpropamide toxicity characterized by obstructive hepatitis, ulcerative proctocolitis, and generalized exfoliative dermatitis which occurred while the patient was taking recommended therapeutic doses of the drug.

Report of a Case

A 53-year-old woman was admitted to the Newark Beth Israel Hospital on June 5, 1959, with complaints of anorexia, diarrhea, and a skin rash. About two weeks prior to admission she had seen her family physician because of weakness, an undetermined amount of weight loss, and pruritus vulvae. Mild hyperglycemia and glycosuria were detected, and she was started on therapy with chlorpropamide. She took 500 mg. for five consecutive days and then 250 mg. daily. About 10 days after initiation of this therapy, the patient noted a blotchy, red rash which began on the anterior chest wall and spread, successively, to the back, shoulders, arms, abdomen, and thighs. This eruption was severely pruritic, and shortly after its onset the patient became aware of alternating hot and chilly intervals. Her temperature ranged between 101 and 103 F (38.3 and 39.4 C), determined orally. In addition, she complained of a cough productive of a clear, watery sputum. Two days after the onset of these symptoms, she returned to her physician, who discontinued chlorpropamide therapy and prescribed an orally given antihistaminic. This afforded some relief from the pruritus, but the other symptoms persisted unabated, and admission to the hospital was advised. She had apparently been in good health prior to the present illness and denied recent injections or exposure to hepatotoxic agents other than chlorpropamide.

On admission, she appeared to be dehydrated and in a toxic state. Rectal temperature was 102 F (38.9 C), radial pulse 126 per minute, blood pressure 100/65 mm. Hg, and respirations 30 per minute. The sclerae were markedly icteric, and hemorrhagic necrotic areas were noted in the mucous membranes covering the palate, uvula, and posterior part of the pharynx. Tender, matted anterior and posterior cervical lymph nodes were palpated bilaterally. The liver was palpated 4 cm. below the right subcostal margin in the midclavicular line and was nontender and semifirm. A diffuse maculopapular eruption covered the chest, back, arms, abdomen, and thighs. Rectal examination revealed exquisite tenderness in all areas, and stool coated with red blood was noted on the examining finger.

Initial laboratory studies revealed a mild eosinophilia and evidence of an obstructive type jaundice (see table). A consultant in dermatology suggested that the skin and mucous membrane lesions represented erythema multiforme secondary to drug toxicity. Proctosigmoidoscopy revealed marked edema, friability, and multiple small ulcerations of the mucosa of the rectum and sigmoid compatible with a toxic ulcerative proctocolitis. A percutaneous liver biopsy was interpreted as showing cholestasis manifested by clusters of dilated bile capillaries containing bile plugs. There was evidence of liver cell regeneration, although no necrosis nor significant degeneration was noted. Two days after admission the patient had a sudden, severe rectal hemorrhage, which was treated with replacement of 1,000 ml. of whole blood.

Because of her rapidly progressive downhill course, she was placed on therapy with prednisone (Meticorten), 40 mg. daily, three days after admission. Shortly thereafter gradual improvement was noted. Her diarrhea ceased two weeks later, and the jaundice cleared one month after her admission (see table). Her skin lesions progressed to a generalized exfoliative dermatitis. After about five

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From the Medical Service, Newark Beth Israel Hospital.

weeks of steroid therapy she was noted to be having active hallucinations. The psychosis persisted for one week after discontinuation of steroid therapy. At the time of this writing she is asymptomatic with normal liver function chemistries and blood cell count (see table). Her diabetes is well controlled with 20 units of N. P. H. insulin daily.

Comment

This case is of interest because of the unusual severity and multiplicity of the toxic effects of therapeutic doses of chlorpropamide. Obstructive hepatitis, erythema multiforme, and exfoliative dermatitis have been described previously, but, to our knowledge, this is the first report of a toxic ulcerative proctocolitis attributable to this drug.

Obstructive Hepatitis.—This case conforms to previously described instances of jaundice attributable to chlorpropamide toxicity.[10] There was biochemical evidence of obstructive hepatitis, and the predominant feature of the liver biopsy was cholestasis.[11] However, in the earlier reports, the jaundice was usually transient and was treated with conservative measures. This patient apparently is the first in whom steroid therapy was necessary. The possibility that this picture was caused by an unrelated viral hepatitis is unlikely because of the associated eosinophilia, cutaneous and colonic lesions, and negative history for exposure to hepatotoxic agents.

Results of Laboratory Studies in Patient with Chlorpropamide Toxicity

Date*	White Blood Cell Count, 1,000 per Cu. Mm.	Polymorphonuclear Cells, %	Stab Cells, %	Lymphocytes, %	Monocytes, %	Eosinophils, %	Cholesterol Level, Mg. per 100 Ml.	Cholesterol Esters, Mg. per 100 Ml.	Bilirubin Level, Direct, Mg. per 100 Ml.	Bilirubin Level, Total, Mg. per 100 Ml.	Alkaline Phosphatase Level, Bodansky Units per 100 Ml.	Cephalin Flocculation, 24 Hr./48 Hr.	Serum Glutamic Oxalacetic Acid Transaminase Value, Units per Ml.	Serum Glutamic Pyruvic Acid Transaminase Value, Units per Ml.	Sulfobromophthalein Retention, % in Blood After 45 Min.
6/6	13.3	33	6	48	10	9	252	211	16.2	21	31.9	1+/1+	166	370	..
6/12	18.3	51	8	30	6	14	250	188	11.1	14	36.0	1+/1+	147	360	..
6/15	..	..	..	..	..	..	...	...	8.7	12	37.6	...	84	254	..
6/21	11.0	69	7	23	1	0	...	...	3.3	4.5	31.7	...	71	115	..
7/8	..	..	..	..	..	..	...	...	0.75	1.0	23.8	1+/1+	24	116	32
7/14	10.7	54	6	31	1	0	200	160	0.3	0.4	10.0	Neg/1+	8	21	..
7/20	8.2	66	2	28	4	0	...	...	0.15	0.5	7.1	...	5	25	†

* Prednisone therapy was begun on June 8 and discontinued on July 15.
† All dye removed from blood.

Cutaneous Lesions.—In previously described instances of erythema multiforme[2a] and exfoliative dermatitis attributable to chlorpropamide toxicity, prompt disappearance of these lesions was noted after discontinuing the drug therapy. In our patient, the erythema multiforme persisted for nearly a month after discontinuation of chlorpropamide therapy and eventually was replaced by a generalized exfoliative dermatitis.

Ulcerative Proctocolitis.—Ulcerative proctocolitis has not been previously reported as a manifestation of chlorpropamide toxicity. Painful bloody diarrhea was one of our patient's most disturbing symptoms. It eventually resulted in severe rectal hemorrhage. The symptoms and sigmoidoscopic evidence of toxic ulcerative proctocolitis cleared after two weeks of intensive steroid therapy.

Addendum

Since this paper was written, Brown and associates have reported three cases of hepatic damage which occurred during chlorpropamide therapy (*J. A. M. A.* **170**:2085-2088 [Aug. 22] 1959). These were relatively mild and responded to mere discontinuation of the drug therapy.

201 Lyons Ave. (Dr. Rothfeld).

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8. References 2*a* and 5.

9. References 2*b* and 5.

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11. References 3*a* and 6*b*.

12. De Salcedo, I., and Borges, F.: Clinical Results of Treatment of Diabetes Mellitus with Chlorpropamide, Ann. New York Acad. Sc. **74:**891-899 (March 30) 1959. Signorelli, S.: Tolerance for Alcohol in Patients on Chlorpropamide, ibid. 900-903. Reference 1*c* and 10*a*.

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USE OF INTRAVENOUSLY GIVEN HYDROXYZINE FOR SIMPLE PAIN-PRODUCING OFFICE PROCEDURES

Theodore Cornbleet, M.D., Chicago

There are many pain-producing procedures in dermatological practice for which it is impractical to use local blocking agents or general anesthesia. These occasions are unpleasant trials for the physician as well as the patient, especially when the latter is a child. Under such circumstances, an agent would be useful that could improve the patient's cooperation by allaying anxiety and apprehension and reducing hypermotility. It should, of course, be safe and preferably act quickly and for a short time without undesirable side-reactions. These criteria appear to be fulfilled by the use of intravenously given hydroxyzine hydrochloride (Vistaril).

Chemistry and Pharmacology

Hydroxyzine is classified as a piperazine and sometimes a diphenylmethane derivative. It has ataractic activity. In pharmacological doses it is nontoxic and well tolerated.[1] In mice, it decreases the motor activity and potentiates the anesthetic effect of hexobarbital. Intravenous injection in mice and rabbits induces a state of hypotony of limbs and neck and quietness without impairing consciousness or interfering with reflexes. These effects begin within two minutes after the injection and last about eight minutes. Hydroxyzine has a protective effect against histamine, serotonin, and acetylcholine aerosols in sensitized animals.[2] It has been suggested that it is useful in controlling anxiety, tension, apprehension, and psychomotor agitation.

Method of Use

In adults, a solution containing between 25 and 50 mg. of hydroxyzine diluted in two or three times as much saline solution or water is injected slowly intravenously. (The larger dose is for corpulent adults.) A boy 12 years of age may be given 15 mg. A dose of 10 mg. was found safe for children aged 3 or 4 years. It acts quickly and its effects subside in a short time. The patient is relaxed and ready for simple dermatological procedures within 10 minutes. Within 30 minutes to an hour after intravenous administration of the drug the patient is ready to leave the office, apparently without much drowsiness or other state which could be hazardous for driving or getting about on foot in busy streets. Few minor dermatological procedures, such as cauterizing or fulgurating warts and moles, require more than 10 minutes, well within the interval during which intravenously given hydroxyzine remains active in the human being.

Results

Forty-three patients (8 children; 35 adolescents and adults) were given intravenous injections of hydroxyzine before submitting to painful minor dermatological procedures. The children were more docile, protested less, and required little or no restraint when the drug was used. Adults permitted painful measures for a longer time before complaining. In 19 patients part of the operation was done before the drug was given. Sixteen of these found the pain was more tolerable after intravenous administration of hydroxyzine. Five others were

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From the departments of dermatology, University of Illinois College of Medicine and Cook County Hospital.

given saline injections intravenously before the first half of the operation followed by hydroxyzine before the second half. Four of them found the latter part less painful. Three were given hydroxyzine and operated on on one day and had the procedure continued on another without use of the drug. All three patients said they felt more pain without the ataraxic. Two complained because they had not been given a "pain-easer" again.

Among the 43 patients, 17 had warts, 3 had molluscum contagiosum, 16 had nevi, 2 had epitheliomas, 2 had sebaceous cysts, and 3 had fibromas. No side-effects were noted. All left the office without troublesome drowsiness. Hydroxyzine induced no increase in bleeding or other apparent untoward effects or lesions on the skin during or after the operative procedures, nor did it retard healing.

Comment

In many instances in which painful minor surgery is done in the office, one is not equipped to administer an anesthetic or it may be undesirable to do so. The use of such an ataractic and psychotherapeutic agent as hydroxyzine under these circumstances may be convenient and simple, facilitate work, and be greatly appreciated by the patient. The drug's rapid and short action too is an advantage. Naturally, when intense pain is felt during an operation stronger anesthetics may be desirable. When only one or a few lesions are to be worked on, they can be infiltrated with a local anesthetic. The method described is suitable for only the simplest office procedures which produce moderate pain for a short time. This report does not include work in which the so-called dermabrasion operation was done, although preparation of the patient with intravenously given hydroxyzine may be desirable for that procedure also.

Summary

Hydroxyzine hydrochloride (Vistaril), an ataraxic and psychotherapeutic agent, was given intravenously to 43 office patients on whom minor, painful dermatological procedures were carried out. Most patients experienced less pain and were more submissive when the drug was used. There were no untoward effects.

30 N. Michigan Blvd. (2)

The hydroxyzine hydrochloride used in this study was supplied as Vistaril by Chas. Pfizer & Co., Inc., Brooklyn, N. Y.

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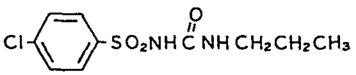
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Chlorpropamide (Diabinese).—1-Propyl-3-(*p*-chlorophenyl) sulfonylurea.—The structural formula of chlorpropamide may be represented as follows:



Actions and Uses.—Chlorpropamide, an arylsulfonylurea, is an orally active hypoglycemic agent which is used for the management of selected patients with diabetes mellitus. The pharmacological actions and clinical uses of chlorpropamide are essentially the same as those of the closely related compound, tolbutamide, and both drugs are believed to influence blood sugar levels by the same basic mechanism of action. (See the monograph on tolbutamide in New and Nonofficial Drugs.) Chlorpropamide is rapidly absorbed from the gastrointestinal tract; the drug is detectable in the blood within one hour after a single orally administered dose, and blood levels are maximal within two to four hours. Because it is excreted very slowly mostly in unchanged form by the kidney, blood levels of chlorpropamide are maintained for considerably longer periods of time than with tolbutamide. This persistence in the body results in a sustained hypoglycemic action. Consequently, doses one-fourth to one-half as great, given less frequently, will produce the same control of the blood sugar level. In this sense, chlorpropamide may be considered more potent than tolbutamide. This in itself should not be construed to indicate that chlorpropamide is more effective. However, certain clinical evidence and laboratory determinations in the form of comparative blood sugar levels within four hours after single-dose administration is also available to indicate that, on an equivalent dose and blood level basis, chlorpropamide has a somewhat greater therapeutic effect than has tolbutamide. This enhanced pharmacological potency may be a factor, along with the delayed excretion, in the production of the desired therapeutic effect with lower, less frequently administered dosage.

Clinical experience with chlorpropamide is presently much less than with tolbutamide. Nevertheless, it is already apparent that both drugs have the same general usefulness. Thus, satisfactory control of the diabetic state with chlorpropamide can be anticipated chiefly in those patients with uncomplicated diabetes mellitus of the stable, nonketotic, maturity-onset or adult type which cannot be controlled by dietary restriction alone. Chlorpropamide may reduce the amount of insulin needed by some patients with juvenile or growth-onset type of diabetes, or unstable or "brittle" type of diabetes, thus permitting a more satisfactory 24-hour control of hyperglycemia than is possible with insulin alone. Like tolbutamide, it is of no value or is contraindicated in patients with diabetes complicated by ketosis, acidosis, diabetic coma, fever, severe trauma, gangrene, Raynaud's disease, or serious impairment of thyroid, renal, or hepatic function. The drug can be used successfully for controlling hyperglycemia in diabetic patients who initially or secondarily fail to respond to tolbutamide.

The criteria used to select candidates for therapy with chlorpropamide are the same as those set forth for tolbutamide. Therapy with chlorpropamide should be undertaken with the same caution as with tolbutamide. Careful instruction of the patient, insistence on rigid adherence to dietary restrictions, and meticulous follow-up observations —all essential for the safe and efficacious use of tolbutamide—are equally necessary with use of chlorpropamide.

In general, all of the side-effects and untoward reactions previously reported with tolbutamide have been observed with chlorpropamide. Although the over-all incidence of these effects is low, most investigators indicate that they tend to occur somewhat more frequently with chlorpropamide than with tolbutamide. It is to be noted, however, that average doses of chlorpropamide considerably in excess of those now recommended and found clinically effective were believed necessary in the early clinical investigations, and, as a result, the reported incidence of toxicity may be unduly high. The influence of lower dosage levels now being used to decrease the incidence of toxic effects remains to be seen. In addition, there is considerable evidence that all sulfonylurea compounds interfere, to some degree, with certain enzymatic processes within the liver; in this respect chlorpropamide is similar to tolbutamide in that both should be administered with extreme caution, if at all, to patients with a history of hepatic dysfunction, with frank jaundice or liver disease being an obvious contraindication. A low incidence of completely reversible jaundice on the basis of intracanicular biliary stasis in association with chlorpropamide therapy has been reported. Accordingly, although transient alterations of alkaline phosphatase are often observed after institution of chlorpropamide therapy, a persistent, serially rising level constitutes an indication for withdrawal of therapy.

Although hypoglycemia of a serious degree has, on occasion, been reported after the administration of tolbutamide, such reactions are more readily produced by overdosage of chlorpropamide. The exaggerated hypoglycemic effect is most likely to occur during the transition period from insulin, but it is a potential danger at any time when there is careless manipulation of dosage. Because of the prolonged action of chlorpropamide, if a hypoglycemic reaction occurs, the patient should be treated with glucose and observed over a period of time to guard against the reappearance of a hypoglycemic episode. To avoid the occurrence of hypoglycemia, the correct dose of chlorpropamide should be given preferably as a single dose with or before breakfast. Chlorpropamide should not be given in the evening without meals. Also, because of its increased potency, chlorpropamide shows a certain similarity of effect to insulin in that the margin of safety between doses producing euglycemia and hypoglycemia is smaller than with tolbutamide. Hence, with chlorpropamide, as with insulin, it is imperative that there be a careful initial adjustment of dosage, as well as adequate orientation of the patients concerning hypoglycemic reactions and their control and the necessity of regular, thorough, follow-up examinations.

It is still too early to make a final assessment of the comparative merits of chlorpropamide and tolbutamide. Presently available evidence, however, would suggest that the advantages of chlorpropamide are threefold: 1. It may be useful in some patients who are originally or who may become unresponsive to tolbutamide. 2. It may make possible a somewhat smoother control of blood sugar. 3. Its prolonged action makes it more convenient to use, i. e., less frequent administration of smaller doses. On the other hand, chlorpropamide has several disadvantages when compared with tolbutamide. These are (1) a slightly higher clinical toxicity and a smaller margin of safety with respect to production of hypoglycemia and (2) the possibility of jaundice.

Dosage.—Chlorpropamide is administered orally. The total daily dosage is generally administered as a single dose each morning with breakfast. Occasional cases of gastrointestinal intolerance may be relieved by dividing the daily dose.

The initial daily dosage for middle-aged patients with mild to moderately severe diabetes should be 250 mg. or less. Because the geriatric diabetic patient appears to be more sensitive to the effects of hypoglycemic agents, consideration should be given to starting older patients on smaller amounts of chlorpropamide.

No transition period is necessary when transferring patients from other oral hypoglycemic agents to chlorpropamide therapy. The administration of the other agent may be discontinued at once and therapy with chlorpropamide started. Although insulin therapy should not be stopped abruptly in the severe or brittle diabetic patient or in the patient receiving over 40 units of insulin per day, the majority of middle-aged patients with mild to moderately severe, stable diabetes who receive insulin can be placed directly on chlorpropamide and their insulin therapy discontinued at once. For patients requiring more than 40 units of insulin daily, chlorpropamide therapy may be initiated with a 50% reduction in insulin for the first few days, with subsequent reductions of insulin dependent upon the response to chlorpropamide.

During the period of insulin withdrawal, the patient should be instructed to test his urine for sugar and ketone bodies at least three times daily and report the results daily. In some cases, it may be advisable to consider hospitalization of the patient during the transition period.

Three to five days after initial therapy, the blood level of chlorpropamide reaches a plateau. The dosage may be increased or decreased by 50 to 125 mg. at intervals of three to five days to obtain optimal control.

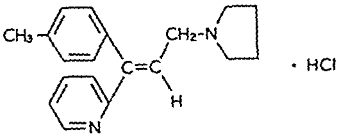
Most middle-aged patients with moderately severe, stable diabetes are controlled by about 250 mg. of chlorpropamide daily. Patients with mild diabetes may do well on daily doses of 100 mg. or less. Many persons with more severe diabetes may require 500 mg. daily for adequate control. Patients who do not respond completely to 500 mg. will usually not respond to higher doses. Maintenance dosage above 750 mg. daily should be avoided.

Preparations.—tablets 100 mg. and 250 mg.

Year of introduction: 1958.

Eli Lilly & Company and Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of chlorpropamide.

Triprolidine Hydrochloride (Actidil).—*trans*-2-[3-(1-Pyrrolidinyl)-1-(*p*-tolyl)propenyl]pyridine hydrochloride.—The structural formula of triprolidine hydrochloride may be represented as follows:



Actions and Uses.—Triprolidine hydrochloride is an antihistaminic agent with actions and uses similar to those of other drugs of this group. (See the general statement on histamine-antagonizing agents in New and Nonofficial Drugs.) After a single oral dose, effects are perceptible within 15 minutes and persist for four to eight hours.

No serious adverse effects have resulted from the clinical use of triprolidine hydrochloride. The incidence of minor side-effects is comparable to that associated with other antihistaminic agents; patients should be advised that drowsiness may occur.

Chronic toxicity studies in animals have disclosed no untoward effects on renal, hepatic, or hematopoietic function. On the basis of a single experiment in which the drug increased the volume and acidity of histamine-induced gastric secretion, it has been suggested that triprolidine hydrochloride be used only with caution in patients with a history of peptic ulcer. However, a similar effect has been observed with other antihistaminic agents, and there is no evidence that triprolidine hydrochloride produces a greater degree of gastric irritation than do other drugs of this group.

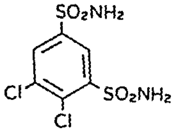
Dosage.—Triprolidine hydrochloride is administered orally, usually three times a day. The usual single dose for adults is 2.5 mg.; for children over two years of age, 1.25 mg.; and for infants, 0.6 mg.

Preparations.—syrup 0.25 mg. per cc.; tablets 2.5 mg.

Year of introduction: 1958.

Burroughs Wellcome & Co. (U. S. A.) Inc., cooperated by furnishing scientific data to aid in the evaluation of triprolidine hydrochloride.

Dichlorphenamide (Daranide).—1,2-Dichloro-3,5-disulfamylbenzene.—The structural formula of dichlorphenamide may be represented as follows:



Actions and Uses.—Dichlorphenamide is a carbonic anhydrase inhibitor with pharmacological actions similar to, but not identical with, those of acetazolamide and ethoxzolamide. On the basis of its ability to inhibit carbonic anhydrase in vitro and on the basis of dosage requirements for comparable pharmacological effects in human beings, dichlorphenamide appears to be one of the most potent drugs of this class currently available. After oral administration, it causes an increased urinary excretion of electrolytes accompanied by diuresis. Sodium and, to a slightly lesser extent, potassium are the principal cations affected. Of the anions, the excretion of bicarbonate predominates. Thus, dichlorphenamide produces a copious flow of slightly alkaline urine. In contrast to other carbonic anhydrase inhibitors, the drug also causes a definite increase in chloride excretion. As a result, metabolic acidosis is less frequent and less pronounced than with other agents of this type. The diminished likelihood of metabolic acidosis is responsible, in part, for two additional characteristics which distinguish dichlorphenamide from other carbonic anhydrase inhibitors: 1. Patients generally continue to show diuretic effects upon repeated administration of the drug. 2. Its anticonvulsant effects are considerably less than with acetazolamide or ethoxzolamide, thus rendering the drug relatively ineffectual for the treatment of epilepsy.

Dichlorphenamide is well absorbed from the gastrointestinal tract. Its distribution, metabolic fate, and excretion are not known.

Although dichlorphenamide appears to be a moderately effective diuretic agent, its clinical use is presently restricted to the treatment of glaucoma. The drug lowers intraocular pressure in normal and most glaucomatous human eyes by reducing the rate of secretion of aqueous humor. In patients responsive to the drug, intraocular pressure begins to fall within one hour after oral administration, reaches a minimum level within two to four hours, and is maintained at a reduced level for 6 to 12 hours. Dichlorphenamide has been used for short-term administration in the management of acute (narrow angle or angle closure) glaucoma and for the acute phase of secondary glaucoma. It is occasionally successful in patients who are refractory to acetazolamide or ethoxzolamide. In some patients with acute glaucoma, however, neither intraocular pressure nor aqueous flow responds to any form of medical management; in these cases, prompt surgery may be mandatory. In all types of glaucoma, dichlorphenamide may be tried for the short-term preoperative control of intraocular tension.

As with any carbonic anhydrase inhibitor, the long-term use of dichlorphenamide for the treatment of chronic congestive glaucoma or chronic simple (wide-angle) glaucoma should be approached cautiously. At the present time, clinical experience with the drug for this purpose is too limited to permit definite conclusions as to its ultimate usefulness. In long-term use, the possible occurrence of serious electrolyte depletion should be borne in mind.

Irrespective of the type of glaucoma being treated with dichlorphenamide, emphasis should be placed on the concomitant administration of standard miotics, particularly in primary glaucomas. It is conceivable that true hypersecretion glaucoma with no obstruction to outflow could be treated with dichlorphenamide or other carbonic anhydrase inhibitors alone until the cause of the hypersecretion has been removed.

Toxicity and Side-Effects.—In the doses required for adequate control of intraocular pressure, the nature and frequency of side-effects due to dichlorphenamide are about the same as those due to acetazolamide or ethoxzolamide. Among these are anorexia, nausea, vomiting, confusion, ataxia, tremor, tinnitus, dizziness, paresthesias, depression, and lassitude. In rare instances, hypersensitivity may be manifested by pruritus, urticaria, and erythematous rash. If therapy is to be prolonged, it is essential to keep a close check on electrolyte balance. Hypokalemia, in particular, must be guarded against, since clinical signs and symptoms of this condition are often insidious in onset. Should this occur, an appropriate potassium salt given orally can usually be administered simultaneously without interfering with the ocular effects; if hypokalemia is severe, further medication should be temporarily discontinued. Dichlorphenamide must be used cautiously in patients with respiratory disorders characterized by a severe reduction in pulmonary ventilation. As with other carbonic anhydrase inhibitors, the drug is contraindicated in patients with hyperchloremic acidosis, adrenocortical insufficiency, and renal failure. Although dichlorphenamide is a sulfonamide derivative, there is no evidence to date of hematopoietic depression or adverse effects on the kidney.

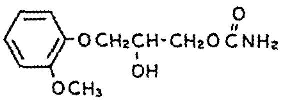
Dosage.—Dichlorphenamide is administered orally. The proposed dosage for adults is an initial dose of 100 to 200 mg., to be followed by 100 mg. every 12 hours until the desired response has been obtained. A dosage of 25 to 50 mg. one to three times daily may be employed for maintenance therapy. Adjustment of dosage to the needs of the individual patient is important.

Preparations.—tablets 50 mg.

Year of introduction: 1958.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of dichlorphenamide.

Methocarbamol (Robaxin).—2-Hydroxy-3-*o*-methoxyphenoxypropyl carbamate.—The structural formula of methocarbamol may be represented as follows:



Actions and Uses.—Methocarbamol is a centrally acting skeletal muscle relaxant similar in pharmacological properties to mephenesin carbamate. The indications for the use of methocarbamol are the same as for other drugs of this group, but its relative value in comparison with other such agents remains to be established by further clinical trial.

Methocarbamol has been found useful in relieving the acute muscle spasm associated with trauma, herniated intervertebral disks, torticollis, and fibromyositis, and in facilitating reduction of dislocations of the shoulder. It sometimes reduces the spasticity, but rarely the athetoid movements, of cerebral palsy. Evidence concerning its effect on the tremor and rigidity of paralysis agitans (Parkinson's syndrome) is conflicting. It is relatively ineffective in combating chronic muscle spasm, such as that accompanying chronic arthritis and persistent back pain, or in relieving the spasticity of multiple sclerosis and the contractures of muscular dystrophy.

Plasma concentrations of methocarbamol reach their peak about one hour after oral administration, as compared to 30 minutes for mephenesin. Plasma levels are also more sustained than those of mephenesin when equimolar doses of the two drugs are administered. The greater persistence of methocarbamol in the blood is apparently not caused entirely by slower intestinal absorption, since it can be demonstrated after intravenous injection as well.

The experimental observation that methocarbamol, in small doses, markedly depresses multisynaptic, but not monosynaptic, spinal reflexes suggests that it acts primarily on the internuncial neurons of the spinal cord. However, the fact that it prolongs the sleeping time of animals given hexobarbital indicates an additional effect on the higher centers. Methocarbamol protects animals against the convulsive effects of strychnine, pentylenetetrazol, or electroshock.

Although about 10% of the patients receiving methocarbamol report unpleasant symptoms or reactions, these are usually mild. Drowsiness, vertigo, blurred vision, headache, nausea, fever, and skin eruptions have been observed. Subjective complaints often disappear with continued medication or may be controlled by a reduction in dosage. Intramuscular injection may produce local irritation. Intravenous administration has been followed by flushing, nausea, metallic taste, and, in one patient, by decrease in blood pressure and bradycardia.

In the early trials of methocarbamol, three cases of transient leukopenia, in which the blood cell count returned to normal despite continuation of therapy, were reported. However, in the subsequent extensive use of the drug, no further instances of this complication have been reported. No serious blood dyscrasias have occurred.

Experiments in animals indicate that methocarbamol, upon intravenous administration, may cause intravascular hemolysis. However, it appears to be less active in this respect than mephenesin, and recommended doses, injected slowly, appear to have only minimal, if any, hemolytic action.

Commercial preparations of methocarbamol may utilize polyethylene glycol as a solvent. Since the latter substance has been reported to increase existing acidosis and urea retention in patients with renal impairment, preparations utilizing this vehicle should not be administered to patients with known or suspected renal disease.

There are no known contraindications to the oral use of methocarbamol. However, patients should be advised that drowsiness and vertigo occasionally occur and that, when these symptoms are present, operation of motor vehicles or other activities requiring mental alertness and physical skill may be hazardous.

Dosage.—Methocarbamol is administered orally or by intramuscular or intravenous injection. Dosage should be adjusted to meet the requirements of the individual patients. However, for initiating therapy, 1.5 to 2.0 Gm. may be given orally four times daily for 48 to 72 hours. Thereafter, 1.0 Gm. four times daily may be sufficient to maintain any beneficial effects. In children, the oral dosage is proportional to body weight; the total daily dosage should not exceed 30 mg. per pound of body weight.

When given intramuscularly, a single dose, in adults, should not exceed 1 Gm. Not more than 500 mg. should be injected in each buttock. The dose may be repeated at intervals of eight hours. Once the desired degree of muscular relaxation has been achieved, substitution of oral therapy is usually desirable.

It is essential that the rate of intravenous injection of 10% solutions of methocarbamol not exceed 3.0 cc. per minute. Care must be taken that extravasation does not occur, since the solutions cause considerable local irritation. No more than 1 Gm. is given in a single injection; the total daily dose should not exceed 3 Gm. Intravenous therapy should not be continued for more than three days in succession.

Preparations.—solution (injection) 1 Gm. in 10 cc.; tablets 500 mg.

Year of introduction: 1957.

A. H. Robins Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of methocarbamol.

HUMANISM AND MEDICINE.—From its beginnings, medicine has evolved as an art based on moral and aesthetic principles, pursuing the knowledge of man as a whole being, both in his physical and spiritual aspects, to assist him in health and disease. As the scientific phase of medicine developed, knowledge of human nature was deepened and the scope of medicine was enlarged. The good physician serves mankind with generosity, sensitivity, and kindness. Medicine is thus, in essence, humanism—understanding man in historical perspective and social evolution, surrounded as he is by an everchanging environment. With these objectives, medicine today is both a biological and a social science bearing directly on all the complexities of society, including man's beliefs, traditions, ideas, and ways of living.—*World Health for World Peace*, November, 1959.

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CRANBERRIES, CHARCOAL, AND CHICKENS

THE HOLIDAY season has been associated with cranberries (*Vaccinium macrocarpon*) and fowl since the first Thanksgiving offered by the Pilgrims in December, 1621, in appreciation of the bountiful harvest. It is reasonable to presume that wild cranberries were served at this first Thanksgiving since it was held near the town of Plymouth in the domain that was to become the Massachusetts Bay colony, not far from the entrance to Cape Cod, the land of cranberry bogs today. It is more than likely that the taste of wild turkey was enhanced by the addition to the menu of the fruit of this shrub. If turnips and cabbage were included among the vegetables served or mustard was used as a condiment, minute quantities of aminotriazole might have been ingested by the Pilgrims more than 300 years ago.

A threat to the inclusion of cranberries in our Thanksgiving dinner just past received wide publicity early in November when evidence was revealed purporting to show that the use of a herbicide, 3 amino-1, 2, 4-triazole, resulted in traces of this artificial contaminant in some batches of cranberries in commerce. Historically, the herbicide has been studied experimentally since 1954. Beginning in the fall of 1956 the probing studies had progressed sufficiently that analyses of cranberries harvested from test crops were carried out systematically to determine whether any residue of aminotriazole remained on the berries. The cranberry laboratory of the University of Massachusetts, an institution of higher learning under a charter from the commonwealth of Massachusetts, participated in these analytic studies together with laboratories in other states, including those in Wisconsin, the second center for cranberry bogs in America. New Jersey, Washington, and Oregon also produce cranberries that enter into interstate sales.

The analyses begun in 1956 were sufficiently satisfactory in detecting residues of aminotriazole that the United States Department of Agriculture reported this compound suitable for use on cranberries. Eighteen months later, early in November of last year, the implication of this compound as a carcinogen prompted withdrawal of all batched cranberries and cranberry products from the open market. This proved to be sad news for the many Americans who love their tart holiday berries. The alleged carcinogenic activity was based on the antithyroid effect, demonstrated in rats but not in other mammals, that followed the ingestion of relatively huge quantities of the compound for relatively long periods of time. Little stress was placed on the well-documented evidence that aminotriazole occurs naturally in vegetables, notably cabbage, turnips, and broccoli, as well as in mustard, or that the antithyroid action is described in current text books of therapy.

According to the *New York Times,* a reputable newspaper in my experience, there were only 3 batches of cranberries under suspicion out of 202 batches examined initially. The number of batches examined was increased several fold in the next fortnight. Before preparing an editorial on this subject that might have been printed in the issue distributed a few days before Thanksgiving and thus available for physicians who read these editorial pages, it seemed best for me to seek consultation. One consultant was my former technical sergeant of Army days, Chester E. Cross, whose knowledge of cranberries extends over several decades and whose judgment as an agricultural scientist ranks high. Currently he is a professor at the University of Massachusetts and in charge of the cranberry station. If you have never mushed through a cranberry bog on the Cape early in September just before the harvest with Professor Cross, you have missed a real experience in sensing dedication to this low-growing shrub that has caused so much consternation. Until further evidence was forthcoming, it seemed prudent to withhold judgment and to delay the preparation of my impressions of the newsworthy affair. A long wait was not necessary. The *Federal Registry* of November 28, 1959, outlined the requirements for specific labeling of cranberries and cranberry products from the 1958 and 1959 crops. If this stipulation was a little late for last Thanksgiving, it was reassuring for those who looked forward to the inclusion of cranberries in the holiday dinners of Christmas and New Years.

Charcoal—carbon black—came under scrutiny on November 20, 1959. Since few persons are addicted to the eating of licorice or black jelly beans, there was considerably less space devoted in the newspapers to the suspicion cast on carbon black than had been afforded cranberries. Chronologically, it was recorded in the *Federal Registry* of December 9, 1958, that carbon black was a permissible food adulterant. The omission of this substance from the registry one year later brought apprehension to the makers of licorice candy and black jelly beans since each item relies on licorice for flavor but charcoal for the characteristic color. A fortnight after this action a supplementary document by the Food and Drug Administration permitted the processors and the users of charcoal in food and candies a three-month period of grace to produce evidence that burned toast is harmless.

Chickens (iatrogenic capons) were under suspicion for only a few days last month. However, neither poultry producers, manufacturing chemists, nor the chickens themselves had violated any federal regulation. Approximately 1% of the chickens eaten in the United States have been given stilbestrol as a fattening hormone. The implantation of pellets of this hormone under the skin at the base of the skull has been an authorized practice for more than a decade. This produces a desired commercial effect, especially attractive to the consumers in New York City and Los Angeles where the caponettes are sold as a premium item. Recent improved tests revealed that residues of the drug remained in the skin, liver, and kidneys. After this disclosure immediate steps were taken to withdraw the caponettes from commerce and to suspend the sale of stilbestrol to the chicken growers.

When next fall rolls around, we hope that cranberries will be permitted for the festive dinners, that licorice and jelly beans will be for sale at the candy counter, and that southern fried chicken will be a permissible menu item.

J. H. T.

ENEMIES OF INTELLECT

These three great forces of mind and will—Art, Science, and Philanthropy—have, it is clear, become enemies of Intellect not of set purpose, not by conspiracy, but as a result of their haphazard assimilation within the House of Intellect itself. The intellectual class, which ought always to remain independent, even of intellect, has been captivated by art, overawed by science, and seduced by philanthropy. The damage done by each has been that of heedless expansion combined with a reliance on the passage of time to restore order and decency. But time moves only by blotting out. In the modern riot of art and science and loving kindness, Intellect has seen decline the virtues that make it what it is: unity, concentration, communicativeness, and the knowledge of itself.—J. Barzun, The House of Intellect, New York, Harper, 1959.

BLEEDING AND CLOTTING TIMES

Current physiological knowledge does not suffice to explain the difference between bleeders and nonbleeders. This was strikingly shown by Ulin and his associates[1] in painstaking clinical observations on the relation of hemorrhage to massive transfusions. The mechanisms normally responsible for the clotting of blood present a tangle of problems that have gone unsolved too long. Every cerebrovascular accident and every postoperative thrombosis or hemorrhage is a reminder of the need for conclusive work in this field.

These problems confront the medical student early in his courses in biochemistry and physiology, when he is required to give coherent answers to examination questions on theories of coagulation. These theories were hard enough to comprehend in 1918; the vocabulary then was limited to a few terms like fibrin, thrombin, antithrombin, and antiprothrombin. The ensuing 40 years of research brought not a clarification of the subject but a profusion of new terms like proaccelerin, factor VII, cothromboplastin, antihemophilic factor B, thromboplastic plasma component, autoprothrombin II, and the Christmas factor. This last embodied more than the usual annoyances of eponymic phrases; the Christmas factor was something involved in Christmas disease, which was defined as a disease caused by deficiency of the Christmas factor in the blood, both the factor and the disease being named after a boy named Christmas. The plethora of words is an outstanding illustration of the fact that disregard for semantics can effectively hinder progress in medical science. An effort is now being made to correct this situation.[2]

The confusion was not, however, entirely semantic and it was not of recent origin. It is now known that some of the substances involved in clotting act in extremely low concentrations, are strongly adsorbed on the surfaces of beakers and other laboratory glassware, and are in some instances fairly stable. Mistaken results have sometimes been traced to the carrying-over of such substances from one experiment to the next by inadequately cleaned apparatus. Publications that make no mention of the precautions taken to insure inactivity of the glassware cannot be trusted. This fact casts a shadow of doubt over much of the older literature on coagulation, the exceptions being the few elementary experiments that could be repeated in the laboratory by students of physiology. Other sources of error less readily identified have undoubtedly contributed to the confusion. Apparently trivial differences between procedures used in different laboratories sometimes led to serious discrepancies in results. The resulting misunderstandings were well summarized by F. D. Mann, in a review of the subject, when he said that it would be "as difficult for eight molecules to get together on one point as for eight coagulationists."[3]

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[1] Ulin, A. W.; Gollub, S. W.; Winchell, H. S.; and Ehrlich, E. W.: Hemorrhage and Massive Transfusion, J. A. M. A. **168**:1971-1973 (Dec. 13) 1958.

[2] International Committee on Nomenclature of Blood Clotting Factors: Four Factors, Their Characterization and International Number, J. A. M. A. **170**:325-328 (May 16) 1959.

[3] Mann, F. D.: Blood Clotting, Ann. Rev. Physiol. **19**:205-230, 1957.

[4] Wilder, J.: Paradoxic Reactions to Treatment, New York J. Med. **57**:3348-3352 (Oct. 15) 1957.

[5] (*a*) Clark, W. G., and MacKay, E. M.: Absorption and Excretion of Rutin and Related Flavonoid Substances, Report to Council on Pharmacy and Chemistry, J. A. M. A. **143**:1411-1415 (Aug. 19) 1950. (*b*) Pearson, W. N.: Flavonoids in Human Nutrition and Medicine, Report to Council on Foods and Nutrition and Council on Pharmacy and Chemistry, ibid. **164**:1675-1678 (Aug. 10) 1957.

[6] Diamond, L. K., and Porter, F. S.: Inadequacies of Routine Bleeding and Clotting Times, New England J. Med. **259**:1025-1027 (Nov. 20) 1958.

[7] Fox, S. L.: Bleeding Following Tonsillectomy and Adenoidectomy, Bull. School Med. Univ. Maryland **38**:134-139 (July) 1957.

The clotting of blood in vitro has thus been sufficiently puzzling, but there have been additional difficulties about the stoppage of bleeding in vivo. The whole subject of hemostasis is made bewildering by the inadequacy of existing tests for bleeding times. It is a matter of record that some tests for bleeding time have been described and widely used in ignorance or disregard of simple modern statistical methods for measuring the reliability of a test. The same has been true of tests for capillary fragility. The consequences of using an unreliable test as a criterion for therapeutic results are or ought to be well known: they are referred to as regression toward the mean, centripetal drift, or the law of initial value.[4] Persons who give extremely high or extremely low values on the first application of an unreliable test generally gravitate toward the normal when the test is repeated. Any therapy can be proved to have a "normalizing effect" if the diagnostic test used is sufficiently unreliable. The history of the flavonoids in therapy[5] can be explained largely in terms of the law of initial value.

The harm resulting from dependence on routine bleeding and clotting times has been brought out with particular clarity by Diamond and Porter.[6] They describe one group of children whose parents had been informed that they had a "bleeding-disease" on the basis of laboratory tests that were falsely positive. In one instance this led to heavy irradiation of the tonsillar area instead of surgery. Another group of patients had serious hemorrhages during or after surgery although no coagulation defects had been demonstrated by the laboratory tests.

What, then, should be the policy of physicians and hospitals with respect to bleeding and clotting tests? From a study of bleeding after tonsillectomy and adenoidectomy, Fox[7] concluded that "We have found little value in making routine bleeding and clotting time determinations, and have discontinued them except when indicated." They are considered to be indicated if the patient gives a history of abnormal bleeding after minor injuries, and if there are familial tendencies toward bleeding. Another authority has described the interest in clotting and bleeding time measurements as a vestige of yesteryear. Yet an uncritical citation of publications out of the past can be used to embarrass a physician who may have decided that such measurements were uncalled for in a given case. When to use and when not to use a particular laboratory test is a scientific, not a legal, question. In connection with determinations of bleeding and clotting time, there is much significance in the bitter remark of one physician. "It would be appalling to me if these procedures must be continued on a mass scale regardless of their lack of scientific value and [their] unreliable and misleading qualities, because it is thought that they have malpractice protection value."

PROJECTS

It says much for the acceptance of foundation of folklore that we all know what a project is: it is something neatly clamped in a folder, not too thin and not too bulky, and typed preferably on an electric typewriter. The last page consists of figures, headed "Estimated Budget" and divided into three- or five-year slices. The project is in truth a literary form, like the Shakespearean sonnet, and its correct composition is an art not vouchsafed to anyone. There is a language appropriate to projects, a tone which veils the diversity of minds, an indefinable fitness to the particular proposal and the promise it holds forth. Just as there is the love sonnet and the meditative sonnet, so there is the problem project and the survey project. Each must follow style and fashion; the idea must be turned in such a way that it shall make the project different from all others, yet "in line with current programs" and at the same time "widely applicable" if successful.—J. Barzun, The House of Intellect, New York, Harper, 1959.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

During the past decade, and especially during the past year or two, numerous governmental and private agencies have made studies of the nation's future needs in medical manpower. As most of you know, the reports by these various groups have presented a wide range of predictions concerning the number of physicians and medical schools required by 1975 and thereafter.

Although opinions differ on the statistical estimates, there is general agreement on the need for constructive planning to meet future requirements. Our population is increasing rapidly. The dimensions of medical knowledge are changing. Medical services are becoming more and more complex. And the American people are showing greater and greater interest in health and medical needs.

Undoubtedly, it will be necessary to bring about a steady increase in the annual number of medical school graduates.

Recognizing all these factors, the A. M. A. House of Delegates in December, 1958, urged existing medical schools to consider the possibility of increasing their enrollments and developing new facilities. It also encouraged the creation of new four-year medical schools and two-year basic science programs by universities which can provide the proper academic and clinical setting. This expansion, it said, should be based on sound, careful analysis of changing needs.

Then, in June, 1959, cognizant of the recruitment problems involved in such expansion, the House of Delegates asked the Board of Trustees to study the possibilities of establishing an A. M. A.-sponsored program of medical scholarships and/or student loans.

Since then, as many times before, I have repeatedly emphasized the need for intensive effort to recruit qualified, dedicated young people into the study of medicine. Superior students are being attracted either by other sciences or by careers which appear to be more lucrative and easily attained. Many are deterred by the cost and length of a medical education.

At the A. M. A. meeting in Dallas last month, the House approved an important recommendation by the Board of Trustees and the Council on Medical Education and Hospitals. It calls for creation of a special committee to "present a scholarship program, its development, administration and the role of the American Medical Association in fulfilling it."

The same committee will study the following seven other major points: (1) the maximum to which medical schools could expand their student bodies while maintaining the quality of medical education; (2) the universities that can support new medical schools with qualified students and sufficient clinical material for teaching—either on a two-year or a full four-year basis; (3) how to obtain competent medical faculties; (4) how to finance the expansion and establishment of medical schools; (5) how to finance medical education in the most economical ways commensurate with high quality training; (6) how to recruit well-qualified students into the study of medicine; and (7) the possibility of relaxing rigid geographic restrictions on the admission of students to medical schools.

I urge the entire profession—including physicians and teachers, medical societies and medical schools —to give full cooperation to the committee's work. It is a constructive effort to plan ahead for the betterment of American health.

Louis M. Orr, M.D.
Orlando, Florida

MEDICAL NEWS

ALABAMA

Conference on Handicapped Children.—The second Alabama Conference on Handicapped Children will be held at the University of Alabama Feb. 11-12. Sponsors of the conference are the Nemours Foundation of Wilmington, Del., and the university. This conference has been planned as a follow-up to the first conference held in Montgomery in November, 1958. The February conference has a two-fold purpose: (1) to provide information concerning speech and hearing disorders and the professions of speech and hearing therapy and audiology, to benefit members of other professions; (2) to promote disciplinary discussion of problems of mutual concern in this area. Guest speakers will have the following topics: Nature and Treatment of Stuttering, Report on a Five-Year Research Project on Cleft Palate, Modern Concepts in the Education of Children with Hearing Loss, Paid on-the-Job Training for Young People with Cerebral Palsy, Ways and Means in Developing a State Program in Speech and Hearing, and the Professions of Speech and Hearing Therapy and Audiology. In addition to general sessions, section meetings are planned. Information may be obtained from Mr. C. E. Adams, Co-ordinator of Conference Activities, Box 2987, University, Alabama.

CALIFORNIA

Dr. Beutler Named Hospital Director.—Appointment of Dr. Ernest Beutler, Chicago, as director of the Hospital for Blood Diseases and chairman of the department of internal medicine, City of Hope Medical Center, was announced by Dr. Paul L. Wermer, Durant, executive medical director. Dr. Beutler has served as assistant professor, department of medicine, and Argonne Cancer Research Hospital, University of Chicago, and is a member of the Subcommittee on Blood Dyscrasias of the Committee on Research, American Medical Association. A diplomate of the American Board of Internal Medicine, he also serves on the editorial board of *Blood, the Journal of Hematology*.

CONNECTICUT

Plan Auditorium at Yale.—President A. Whitney Griswold of Yale University announced a gift of $591,000 from the Commonwealth Fund to construct a 449-seat auditorium at the Yale School of Medicine, New Haven. Groundbreaking is expected to take place this winter and the new auditorium completed by Jan. 1, 1961. The building will be named the Mary S. Harkness Memorial Auditorium after the wife of the late Edward S. Harkness, Yale '97, president of the Commonwealth Fund until his death in 1940. Mrs. Harkness was honorary president of the fund from 1940 until her death in 1950. The auditorium will be located in a courtyard of the Sterling Hall of Medicine. The building will also have conduits for closed-circuit televising of operations and other activities of the medical center.

COLORADO

Survey of Psychiatric Facilities.—Dr. Paul H. Hoch, New York State commissioner of mental hygiene, will come to Denver late in January to survey Colorado's psychiatric facilities. At the invitation of Governor Steve McNichols, Dr. Hoch will study the existing program and make recommendations for reorganization and future development. In Colorado for about 10 days, the commissioner will aid in setting up a long-range mental health program and will consult with Colorado authorities regarding priority of expenditures for physical plant. At present Colorado has one mental hospital of 6,000 beds.

Combined Meeting in Colorado Springs.—The Colorado Region of the American College of Physicians and the Colorado Society of Internal Medicine will hold a combined meeting in Colorado Springs, with headquarters at the Broadmoor Hotel. Dr. John L. McDonald, president, Colorado State Medical Society, will preside at the opening session. The following papers will include invited authors:

The Value of the P wave in Precordial Lead V-1 in Patients with Left Atrial Enlargement, Dr. David E. Dines, Rochester, Minn.

The Cell Cholinesterase in the Diagnosis of Blood Dyscrasias, Dr. Joseph H. Holmes, Denver, and Dr. Prawase Wasi.

Hypertrophic Osteoarthropathy Secondary to Intrathoracic Diseases, Drs. Arthur Evans, Oren B. Gum, and Charley J. Smyth, Denver.

Symposiums will be conducted at the University of Colorado Medical Center, National Jewish Hospital, and Fitzsimons Army Hospital. Question-and-discussion periods are planned. Guest speakers will be Dr. Howard P. Lewis, Portland, Ore., president of the college, and Dr. Carl V. Moore, head, department of medicine, Washington University School of Medicine, St. Louis. A banquet is planned

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

for the evening of Jan. 22. For information, write the American College of Physicians, 4200 Pine St., Philadelphia 4.

Personal.—Dr. Robert J. Glaser, University of Colorado vice-president for medical affairs and dean of the University of Colorado School of Medicine, Denver, was elected to a three-year term on the executive council of the Association of American Medical Colleges. Dr. Glaser was also reelected chairman of the AAMC's Committee on Research and Education.——Dr. Franklin G. Ebaugh, who headed the department of psychiatry of the University of Colorado School of Medicine, Denver, for 29 years, from 1924 to 1953, and who has been a member of the volunteer faculty since that time, has been designated as clinical professor of psychiatry emeritus by the C. U. board of regents. He plans to retire from the faculty post soon.

DISTRICT OF COLUMBIA

Dr. Shilling Honored.—Dr. Charles W. Shilling, deputy director, division of biology and medicine, U. S. Atomic Energy Commission, was presented the Outstanding Achievement Award by the regents of the University of Michigan at ceremonies held Nov. 21. The award, established by the regents in May, 1958, is presented to alumni who are recommended for the honor by the faculties of the university's schools and colleges.

Personal.—Dr. William F. Sheeley, formerly of Hastings, Minn., joined the staff of Dr. Mathew Ross, medical director of the American Psychiatric Association in Washington. He will head the A. P. A.'s General Practitioner Education Program, which is operated with grant support from the National Institute of Mental Health, U. S. Public Health Service.

ILLINOIS

Slide Sets Available.—The Illinois Society of Pathologists announced that there are some seminar slide sets available to those interested, at a cost of $10. Each set includes 11 different cases and 16 slides. Orders should be sent to Dr. James B. Hartney, 410 Lake St., Oak Park, Ill.

Chicago

Annual Lecture.—The second annual Nelson M. Percy Lecture will be given under the auspices of the Nelson M. Percy Research Foundation Jan. 15, 8 p. m., in the auditorium of the Augustana Hospital, 411 W. Dickens. The speaker will be Dr. Erwin R. Schmidt, head of the department of surgery, University of Wisconsin, College of Medicine, Madison. The title of the lecture is "Thirty Years' Experience with Surgical Anesthesia."

Hospital News.—Holy Cross Hospital Blood Bank, 2700 W. 69th St., is a member of the Cooperative Blood Replacement Plan, a public service sponsored by the Chicago Blood Donor Service, Inc. The plan has been developed "as a means of making more blood available for general use and to protect people that give blood." According to Sister M. Theresia, supervisor, an individual can donate a pint of blood at any of the hospitals participating and in return receives, should he need it, an unlimited supply of blood for four years.

Appoint Ophthalmology Research Director.—Dr. Albert M. Potts was appointed professor of ophthalmology in the department of surgery and director of research in ophthalmology at the University of Chicago. Dr. Potts, a member of the faculty of Western Reserve University, Cleveland, since 1948, was associate professor of ophthalmic research from 1954 to 1959. While at Western Reserve University, Dr. Potts in conjunction with the department of anatomy developed a television ophthalmoscope. Dr. Potts will conduct research in toxicology of the eye and in electrophysiology in addition to his teaching and clinical duties.

Surgical Meeting.—The Chicago Surgical Society will meet Friday, Jan. 8, at the Knickerbocker Hotel. The program includes the following papers:

Factors Influencing the Incidence and Mortality of Acute Perforated Gastroduodenal Ulcers, Drs. Carl A. Meyer and Donald D. Kozoll.
Incidence of Carcinoma at the Esophagogastric Junction in Short Esophagus, Dr. Edward A. Stemmer and William E. Adams.
Repair of Tissue Deficient Hernias by Aortic Implants, Drs. Samuel J. Fogelson, Charles R. Jackson, and William J. Norcross.
The Experimental Use of a Vaso-Pressor at the End of Temporary Aortic Occlusion, Drs. Robert P. Hohf and George C. Sutton.

The morning session will be held at the Children's Memorial Hospital. For information, write Dr. Robert L. Schmitz, Secretary, 55 E. Washington St., Chicago 2.

KENTUCKY

Flying Physicians Plan Fly-in.—Kentucky's Flying Physicians are planning their second state-wide fly-in at Kentucky Lake the weekend of Feb. 6-7, according to Dr. Norman K. Cohen, Louisville, corresponding secretary and editor of the group. Their first gathering was held at Owensboro Oct. 18. A program of scientific sessions and free instrument-flight instruction is being arranged by Dr. Max P. Jones, Louisville, program chairman. The instrument-flight instructors are Dr. Marvin A. Bowers Jr., Louisville, and Dr. Francis X. Sommer, Corbin. The Kentucky section of the Flying Physicians Association, numbering some 50 members, is a part of the national organization which was founded in Chicago in May, 1955, and held its first meeting in Atlantic City the following month. Members are available to fly to stricken areas for disaster-relief work.

MASSACHUSETTS

Fund for Research in Neurology.—Part of a gift of nearly $500,000 by the late Katherine E. Bullard to Harvard University provides for research in neurology. At Harvard Medical School, Boston, the Stephen Bullard Memorial Fund will be used for "the advancement of research in neurological development." This fund and a professorship in forestry at Harvard commemorate two brothers of Miss Bullard. The Bullard Professorship of Neuropathology at Harvard Medical School was established by Louisa Norton Bullard and her children in memory of her husband, William Story Bullard, a Boston merchant.

Fellowships in Population Dynamics.—A program of fellowships for advanced study and research in population dynamics has been established at the Harvard School of Public Health, Boston, by an anonymous donor. Two fellowships are available, one for a citizen of the United States and one for a citizen of another country, preferably one in which overpopulation is a particularly serious problem. Awards will be restricted to graduates of approved medical schools or persons with similar preparation in the biological sciences. Students whose native language is not English must demonstrate ability to speak, read, write, and understand the English language. It is intended that a fellow in population studies will enroll initially at the Harvard School of Public Health as a candidate for the degree of master of public health or for the degree of master of science in hygiene, with emphasis on public health methods for the control of overpopulation. If his performance in the first year is satisfactory, the student would be eligible for continuation of fellowship support for an additional year, during which he would engage in research in population dynamics at the Harvard School of Public Health or in the field. Inquiries concerning the fellowship program should be directed to the Registrar, Harvard School of Public Health, 55 Shattuck St., Boston 15. Applications for the academic year beginning Sept. 26 must be received before March 1. Awards will be announced before May 1.

MICHIGAN

Study of Water in Great Lakes.—Sampling of public water supplies at Sault Ste. Marie and Port Huron has been started as part of a long-range study of water quality in the Great Lakes area, the Michigan Department of Health announced. The samples will be tested for radioactivity, plankton, chemicals, and other possible contaminants. The study is aimed at determining how changes in water use and area development affect water quality. Sampling of this kind has been in progress at Detroit for several years. Local water departments are running some of the sampling tests, and others are being made by the U. S. Public Health Service.

Personal.—Dr. Herman D. Scarney, chief of staff of William Beaumont Hospital, Royal Oak, and aviation medical advisor to the General Motors Corporation, was placed on the retired list of the United States Navy Reserve with the rank of rear admiral as of Sept. 1. Admiral Scarney completed over 30 years of service in the United States Navy and was active in the aviation arm of the Navy during World War II. He is assistant clinical professor of ophthalmology of Wayne University College of Medicine, Detroit.——Mr. Duncan M. Laidlaw has been appointed executive director of the Michigan Chapter, Arthritis and Rheumatism Foundation, with headquarters in Detroit. He succeeds Mr. J. Howard Stephenson, who continues with the chapter as a director.

MISSISSIPPI

University Appointments.—The appointment of four physicians to the University of Mississippi School of Medicine faculty was announced. Dr. Paul S. Derian, Charlottesville, Va., was named associate professor of surgery and chief of the orthopedics division, replacing Dr. William F. Enneking, Jackson, who has accepted a professorship in Florida; Dr. Ben B. Johnson, San Francisco, and Julian R. Youmans, Ph.D., were appointed assistant professors of medicine and neurosurgery, respectively (Dr. Johnson heads the division of renal diseases); and Dr. Guiseppe Scarcella, Houston, was appointed instructor in neurosurgery.

NEBRASKA

Foundation for Respiratory Research.—A nonprofit foundation to finance studies of diseases of the respiratory tract has been formed in Omaha. Incorporation papers for the Respiratory Research Foundation were filed with the Secretary of State in Lincoln Dec. 3. Dr. James J. O'Neil, Omaha otolaryngologist, is director of the foundation.

NEW JERSEY

Dr. Grady Named Acting Dean.—The board of trustees of the Seton Hall College of Medicine appointed Dr. Hugh G. Grady as acting dean. Dr. Charles L. Brown, who had been dean since the inauguration of the college in 1956, died Dec. 4. Dr. Grady has been associated with Seton Hall since 1957, when he was appointed a professor and director of the department of pathology. Prior to this he had been scientific director of the American Registry of Pathology of the Armed Forces Institute, Bethesda, Md.

NEW YORK

Child Injury Study Project.—A "Child Injury Project" was begun in Rockland County in September to test the effect of public health education on the incidence of accidental injury to preschool children through controlled study. The project has been made possible through a grant ($121,538) awarded to Rockland County by the National Institutes of Health through the Department of Health, Education, and Welfare. The three-and-one-half year study is under the co-direction of Dr. Donald G. Dickson, health commissioner of Rockland County, and Dr. Edward B. Schlesinger, acting director of the Division of Medical Services of the State Health Department. The project will involve obtaining initial data on injuries to preschool children from physicians and hospitals, conducting a planned education program with one group involved in the study, and evaluating the effect of education on the number of subsequent injuries.

New York City

Physician and Student Win Scholarships.—The American-Hungarian Medical Association awarded scholarships to Dr. Laszlo Biro, New York University ($450) and Miss Judy M. Roheim, medical student, New York City ($350). These scholarships were awarded "in the ever continuing effort of the American-Hungarian Medical Association to help physicians and medical students who seek a new home in this country."

Residency Program in Neurology.—The Bronx Veterans Administration Hospital in affiliation with Columbia University announced an approved three-year residency program in neurology. In addition to work at the hospital, residents spend six months full time at Montefiore Hospital, four months full time in the department of neuropathology at the Columbia-Presbyterian Medical Center, and over a period of 14 months attend various neurologic outpatient clinics of the New York Neurological Institute. Lectures in the basic sciences are given at Columbia University. The training program is under the supervision of Dr. Carl B. Booth in collaboration with Drs. Daniel Sciarra, Abner Wolf, and Tiffany Lawyer, Jr. Candidates who wish to apply for residency may obtain information about the program by writing to Dr. Carl B. Booth, Chief, Neurological Section, Veterans Administration Hospital, 130 W. Kingsbridge Road, Bronx 68, N. Y.

Dedicate Library at Rockefeller Institute.—The Alfred E. Cohn Library of the Rockefeller Institute was dedicated Dec. 3. A memorial service was conducted in honor of the late Alfred Einstein Cohn, cardiologist and member emeritus of the institute, who died July 20, 1957. Participating in the ceremonies were Detlev W. Bronk, president of the institute; Dr. Henry A. Murray, professor of psychology, Harvard University, Boston; Dr. F. Peyton Rous, member emeritus of the institute; and the Hon. Felix Frankfurter, associate justice of the Supreme Court. The Alfred E. Cohn Library, consisting of the books which Dr. Cohn had collected throughout his life, over 6,000 volumes in number, is available to students and faculty members of the institute as well as visiting scientists. There are volumes of scientific interest published in the 16th, 17th, and 18th centuries; many books in medical science issued in the 19th and 20th centuries; and general works in literature, philosophy, history, art, politics, and other subjects. Dr. Cohn was associated with the Rockefeller Institute for 33 years. While working in London with Sir James Mackenzie, he discovered the presystolic murmur. Later, working with Thomas Lewis, Dr. Cohn helped to set up the Einthoven string galvanometer for making electrocardiograms at University College in London.

VIRGINIA

New County Society.—The Prince William County Medical Society was formed at Lake Jackson Lodge by a group of Prince William County physicians and surgeons and its charter granted on Oct. 15 by the Medical Society of Virginia. Dr. Alvin E. Conner, of Manassas, was elected president, Dr. Alfred J. Ferlazzo, of Triangle, was named vice-president, and Dr. Moses L. Nafzinger, of Woodbridge, was made secretary-treasurer. Sixteen charter members formed the new association, which is drawing up its by-laws. Before the society's existence, Prince William County was one of only four counties in the state which did not have a medical society. A primary aim of the newly organized society is to help set up the projected Prince William County Hospital. Its formal objectives are: to promote continuation of education for the physician; to provide opportunity for social contact among physicians; to promote the medical welfare of the county; to provide a means for expressing the unified opinion of physicians; to improve the public relations of the medical profession.

WEST VIRGINIA

Ophthalmology and Otolaryngology Meeting.—The West Virginia Academy of Ophthalmology and Otolaryngology will hold its annual meeting at the Greenbrier Hotel, White Sulphur Springs, April 10-12. The guest speakers will include Dr. Harold G. Scheie, professor of ophthalmology, Pennsylvania University School of Medicine, Philadelphia; Dr. Charles E. Iliff, associate professor of ophthalmology, Johns Hopkins University School of Medicine, Baltimore; and Dr. Oscar J. Becker, clinical associate professor of otolaryngology, University of Illinois, Chicago. For information, write the secretary, Dr. Albert C. Esposito, First Huntington National Bank Building, Huntington 1, W. Va.

Personal.—Dr. Chauncey B. Wright, of Huntington, was reelected president of the West Virginia Cancer Society at the annual meeting held in Huntington Oct. 1.——Dr. Jesse J. Jenkins Jr., of Fairmont, was installed as president of the West Virginia Heart Association. He succeeds Dr. James H. Wolverton Jr., of Piedmont, who has served during the past year.——Dr. John D. Lee, of Dry Creek, Raleigh County, was appointed by Governor Cecil H. Underwood as superintendent of the Andrew S. Rowan Memorial Home at Sweet Springs. He succeeds Dr. Albert Pierce Traynham, resigned. Dr. Lee has been engaged in general practice in West Virginia for the past 35 years.——Dr. Margaret T. Ross, of Charleston, former director of the West Virginia State Department of Mental Health, has been named director and psychiatrist at Hillcrest, a Charleston Mental Health Center for Children.——Dr. William R. Laird, of Montgomery, was awarded the degree of doctor of science by Waynesburg College at Waynesburg, Pa.

GENERAL

Three of One Family Honored.—At the 64th annual convention of the National Medical Association Aug. 10-13, a memorial service was held by the Woman's Auxiliary honoring Mrs. Alma Wells Givens who founded the auxiliary in 1936 and who died in March, 1958. The National Foundation presented to Dr. John T. Givens, Norfolk, Va., executive secretary of the association for 24 years, an illuminated citation for "outstanding achievement and help to the National Foundation in its Polio and Arthritis drives over the many years." The third member of the family to be honored was Dr. John D. Givens, who, in conjunction with Dr. William J. Gillesby, and Dr. Harold A. Paul, of Chicago, were awarded the first cash prize in the resident program—their paper being "The Right-Sided Approach to Carcinoma of the Esophagus."

Meeting of Physicians in Columbus, Ohio.—A combined regional meeting of the American College of Physicians, to include Ohio, Western Pennsylvania, and West Virginia, will be held in Columbus, Ohio, Jan. 28-29. Scientific sessions will be held at the Student Union Ohio State University, and the official hotel will be the Deshler-Hilton Hotel. The program includes clinical pathological conferences and 23 papers in addition to 21 papers to be read by title. Dr. Howard P. Lewis, Portland, Ore., president of the college, will be principal speaker at the banquet Jan. 28, 7 p. m., and a second guest of honor will be Dr. Edward C. Rosenow Jr., Pasadena, Calif., who succeeds Mr. Edward R. Loveland as executive director of the college Jan. 1. Registration fee is $10, with interns and residents admitted free. For information, write Dr. George J. Hamwi, Ohio State University Hospital, Columbus 10, Ohio.

Society News.—At the annual meeting of the **Rocky Mountain Radiological Society** new officers for 1960 were elected as follows: president-elect, Dr. Peter E. Russo, Oklahoma City, Okla.; first vice-president, Dr. John W. Walker, Kansas City, Mo.; second vice-president, Dr. Maurice C. Archer, Fort Worth, Texas; secretary-treasurer, Dr. John H. Freed, Denver. The 1960 meeting will be held in Denver, Aug. 11-13 at the Denver Hilton Hotel.——The officers of the **American Association of Blood Banks** are: president, Dr. Elmer R. Jennings, Long Beach, Calif.; vice-president, Dr. Tibor J. Greenwalt, Milwaukee; secretary, Dr. John B. Alsever, Phoenix, Ariz.; treasurer, Mrs. Bernice M. Hemphill, San Francisco; president-elect, Dr. John R. Schenken, Omaha; and immediate past-president, Dr. Ralph M. Hartwell, New Orleans.

Seminar Cruise to Caribbean.—The Pan-American Academy of General Practice for their annual convention will join with the medical seminar cruise sponsored by the Alumni Association of the New York Medical College. The program will be presented by members of the faculty, including Drs. Ralph E. Snyder, dean; Linn J. Boyd; Frank J. Borrelli; Kenneth R. Crispell; Walter L. M. Wersheimer; David Scherf; Francis D. Speer; and Martin L. Stone. This medical seminar cruise will be held aboard the S S Hanseatic, sailing Feb. 25 and returning March 11, visiting St. Thomas, La Guaira, Curacao, Cristobal, Kingston, and Port-au-Prince. The seminar constitutes 30 hours acceptable category I postgraduate requirements of the A. A. G. P. Application for reservation must be made to Dr. Cassius Lopez de Victoria, Executive Director, Pan American Academy of General Practice, 176 E. 71st St., New York 21.

Grants for Nutrition Research.—New grants totaling $340,000 to 11 university research laboratories across the country for basic research in nutritional science have been announced by the Nutrition Foundation. This raises total awards made by the foundation since its inception in 1941 to more than $5,500,000. Much of the new work underwritten by the foundation will be in fat metabolism. Financed by the food industry and with its research activities guided by an independent scientific advisory committee, the Nutrition Foundation is dedicated to furthering fundamental knowledge in nutrition. To expose food fads and quackery and to inform the public on sound nutritional practices, the foundation has allotted $61,000 in the new grants to the American Institute of Nutrition, the American Medical Association, the National Research Council, the New York Academy of Medicine, the American Dietetic Association, and other professional societies. New grants will go to the following universities: Florida, Wisconsin, Chicago (two grants), Notre Dame, California (U. C. L. A., two grants), Cornell, Wayne State, and Columbia.

Chairman of the Nutrition Foundation is James R. Killian Jr., Sc.D., chairman of the Massachusetts Institute of Technology.

Southeastern Surgeons Meeting in New Orleans.—The 28th annual assembly of the Southeastern Surgical Congress will be held March 21-24 at the Roosevelt Hotel, New Orleans, under the presidency of Dr. Benjamin T. Beasley, Atlanta, Ga. Participants will include the following guest lecturers: Dr. John C. McClintock, Albany, N. Y.; Dr. Charles C. Higgins, Cleveland; Dr. Frank Glenn, New York City; Dr. Alexander T. Bunts, Cleveland; Dr. Jonathan E. Rhoads, Philadelphia; Dr. Denton A. Cooley, Houston. A panel discussion, "Acute Intestinal Obstruction," will be moderated by Dr. William O. Barnett, Jackson, Miss., on March 21, 4:30 p. m. A forum on progress in surgery is planned for the afternoon of March 22. Dr. Willard H. S. Parson, Vicksburg, Miss., will moderate a discussion on operative complications, March 23. For information, write Dr. Benjamin T. Beasley, President and Secretary Director General, Southeastern Surgical Congress, 340 Boulevard, N. E., Atlanta 12, Ga.

Refresher Courses for Medical Librarians.—The third Medical Library Refresher Course Program, sponsored by the Medical Library Association, will be held on Monday, May 16, preceding the association's 59th annual meeting at the Hotel Muehlebach, Kansas City, Mo. The courses are listed as follows: acquisition, administration, bibliography, cataloging and classification, the county medical society library, periodicals, public relations, rare books, reference, the small medical library in the hospital, teaching bibliographic research methods, and weeding. The first six courses will be given at 9 a. m. and the second six will be given at 2 p. m. It is possible to attend only one lecture from each group. Each session will be three hours long, including lecture and discussion. Fees for active and associate members will be $5 for two lectures or $3 for a single lecture. For nonmembers the fee will be $10 for two lectures and $6 for each single lecture. Preregistration is to end April 1. For details, write Mr. Thomas E. Keys, Chairman of the Refresher Course Committee, Mayo Clinic Library, Rochester, Minn.

Health Program for School Children.—Recommending the employment of private physicians as important members of the school health team, the Committee on School Health of the American Academy of Pediatrics has outlined a health program for school-age children. Immunization procedures should, insofar as possible, be done by the patient's private physician or local health department, the committee advised, and schools should not take responsibility for performing the actual immunizations. The school physician, the committee said, is a health adviser instead of a source of medical care. They recommended that the school health team employ private physicians part time and give preservice training courses for them and the entire staff. The team should use standard forms to record examinations and progress, and continuously remind local physicians of the purpose and functions of the school health service. They should make available to private physicians the results of any examinations and appraisals made in the school. The committee suggested that the medical examination be used as an opportunity to promote preventive medicine, health improvement, and health education, rather than solely for the detection of health impairments, and said such a conference should take place in the office of the child's physician. They reported that a school health program should include adequate supervision of the physical, mental, emotional, and social aspects of school life, and the planning of the course content and instruction in nutrition and health education, including accident prevention, recreation, and physical education.

Study in Prostatic Cancer.—As part of a national program in cancer research, a cooperative study in prostatic cancer has been organized among 10 medical centers and is under way under the chairmanship of Dr. Herbert Brendler, department of urology, New York University Medical Center. The objectives of the study are to evaluate the effectiveness of experimental compounds for use in the therapy of patients with advanced, disseminated prostatic cancer and to develop an improved method of cooperative investigation. New York University–Bellevue Medical Center, as the central coordinating agency for the nation-wide study, is responsible for the statistical analysis of data, the evaluation of results, and the publication of reports to cooperating investigators and the Cancer Chemotherapy National Service Center. Other cooperating centers are: Memorial Center for Cancer and Allied Diseases, University of Rochester, Columbia University, and Johns Hopkins University in the East; Northwestern University, the University of Iowa, and the University of Kansas in the Midwest; on the West Coast, the University of Oregon and the University of California at Los Angeles; Vanderbilt University and the University of Miami in the South. The study will be conducted on the experimental and clinical level simultaneously.

Scientists Receive Award for Drug Research.—A research team of nine chemists, a botanist, and six laboratory assistants was presented with the Superior Service Award of the U. S. Department of Agriculture for finding in wild plants a series of compounds known as steroidal sapogenins, and for showing how these compounds could be converted to drugs. The award was presented by

George W. Irving Jr., Ph.D., Washington, D. C., deputy administrator of the Agricultural Research Service, who said the award recognized "almost a decade of outstanding research cooperation." The program, started in 1950, consisted of a search of remote areas of the world for plants containing precursors of cortisone, screening of thousands of such plants in the Wyndmoor laboratory, and chemical conversion to cortisone and other drugs of promising substances found in the plants. Such plants have been shipped to the department's Wyndmoor (Pa.) laboratory, and constituents of many of them have been converted to cortisone by procedures developed at the laboratory. In making the award to the research team, Dr. Irving said the domestic cultivation of drug plants should reduce their cost by removing our complete dependence on foreign imports for them, and also would give American farmers a new crop with which to replace some acreages now adding to our surpluses of certain crops.

Institute for Information on Soviet Research.—Pergamon Institute, a nonprofit foundation, was formed in 1957 for the purpose of making available to English-speaking scientists, doctors, and engineers (from all countries that are members of the United Nations) the results of scientific, technological, and medical research and development in the Soviet Union and other countries in the Soviet orbit. The institute maintains offices in Washington, London, and Oxford. The institute's aim of commissioning a series of review volumes, with complete bibliographies, covering broad areas of Russian scientific medical and technical progress has been paralleled by the decision of the U. S. S. R. Academy of Sciences' Institute of Scientific Information to produce such volumes covering both Soviet and foreign developments. The Pergamon Institute has made arrangements to be kept informed on this series and to receive advance copies. The institute will arrange the translation and publication of all volumes or parts of volumes considered by its scientific advisers to be of interest and value. The Pergamon Institute is also planning publications based on the Express Information Service of the Academy of Sciences, which consists of 48 separate weekly journals covering industrial subjects. The institute announced a program for the preparation of Russian–English scientific and technical dictionaries and glossaries. Plans are being discussed for the preparation of a Chinese–English technical and scientific dictionary. The institute now publishes 18 selected Russian journals in translation. It is assisting with the translation and publication of Russian books on science, technology, and medicine. Institute services available are: listing and abstracting services; bibliographical services; critical evaluation of Russian publications; books, journals, and microfilms; translations—books and journals; translations—articles and extracts; reciprocal services (available to learned societies nd individual scientists throughout the world on same nonprofit basis in return for their coopera-); information service for press, radio, and vision; Soviet patents. For information, write rgamon Institute, 1404 New York Ave., Washington 5, D. C.

FOREIGN

Surgical Conference in Israel.—The minister of health of the State of Israel, and the Israel Section of the International College of Surgeons have announced an International Conference of Surgeons to be held in Tel Aviv and Jerusalem May 21-23, 1960. The conference will follow the 12th biennial international congress of the International College of Surgeons in Rome (May 15-18, 1960). The Israel conference will be held under the auspices of the Ministry of Health. The Israel Section of the International College of Surgeons will co-ordinate scientific and clinical sessions. Special significance will be attached to the surgical and medical problems of young nations. Visits to Israel's leading hospitals and health clinics will be arranged. For details on the Israel Conference write to: Secretariat, International College of Surgeons, 1516 Lake Shore Drive, Chicago.

Commission on Alcoholism Meets in Paris.—The International Commission on Alcoholism in Industry will hold its first session June 8-10 in Paris in association with the Conference of French Industrial Enterprises on Safety at Work and Alcoholism. Study and discussion sessions will be held on (1) safety at work and alcohol; (2) the prevention of alcoholism in industrial establishments: information and education of personnel on alcoholism in industrial establishments; (3) early detection of alcoholics in industrial concerns; and (4) the works doctor—his role in the prevention of alcoholism in the factory and its treatment. The international commission, intended particularly for representatives of industry, trade-union representatives and works doctors, has as its objective the study of different aspects to combat alcoholism in industrial establishments. For information, write Mr. André Bertrand, 24, Bd. Raspail, Paris VIIe, France.

Conference on Medical Electronics in London.—The third International Conference on Medical Electronics will be held in London July 21-27, organized by the Electronics and Communications Section of the Institution of Electrical Engineers and the International Federation for Medical Electronics. The conference will include an equipment exhibit at Olympia. At the second International Conference on Medical Electronics held in Paris in June, 1959, an International Federation for Medical Electronics was organized and executive committee officers were elected, including V. K. Zworykin, Rockefeller Institute, as president. The organizing committee for the third conference has issued a call for four classes of papers: research and advanced development; survey papers; integrating papers which present a critical view of developments in the field; medical electronic engineering practices and achievements. The committee has listed the following sessions:

1.—Instrumentation for Biological Needs.
2.—Medical Electronics in Space Research.
3.—Isotopes and Radiology.
4.—Ultrasonics.
5.—The Respiratory System.
6.—The Digestive System.
7.—The Circulatory System.
8.—Electronic Aids to Sight, Hearing, and Locomotion.
9.—The Nervous System.
10.—Electronic Aspects of Human Engineering.

Interest is in short papers of 300 to 2,500 words which deal with practical problems encountered in the operation of equipment or with limited aspects of a wide subject. A longer paper may be submitted but should not exceed some 8,000 words. Manuscripts must be double spaced and submitted in triplicate. Authors from the United States may submit manuscripts to the Program Coordinator for the United States, Dr. Lee B. Lusted, Department of Radiology, University of Rochester School of Medicine, Rochester 20, N. Y. Deadline for papers is Feb. 15.

CORRECTIONS

Nine Eminent Scientists.—The word "dentists" in the second line of the editorial on page 2332 in The Journal, Dec. 26, 1959, appeared in error; the word should have been "scientists."

Medical Motion Picture Review.—A review of the medical motion picture, "Early Detection and Medical Management of Ulcerative Colitis," was published in the Nov. 28, 1959, issue of The Journal on page 1873. The major premise of the film is that with the early detection of ulcerative colitis and proper medical management surgery can be avoided. Accordingly, the beginning of the third paragraph of the review should have read, "The third major portion of the film is devoted to therapy."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for filing application is January 10. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Oral.* San Francisco, March 30-April 1; New York City, Nov. 14-17. Closing date for filing application is Jan. 2 and July 1. *Written.* Oct. 17. Closing date for filing application is May 1. *Oral. Gastroenterology.* Philadelphia, March 11-12. Final date for filing application is January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part I, Written.* Chicago, January 16. Candidates notified of their eligibility to participate in the Part I examination must submit their case abstracts within thirty days of notification of eligibility. *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral*, Chicago, Oct. 3-7. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. Final date for filing application is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Cincinnati, Spring 1960. Deadline for filing applications was Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Oral Examinations (Part II):* Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Feb. 12. Final date for filing application was Dec. 1. *Oral.* May 1960. Final date for filing application was Dec. 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Abt, A. F. Hugo, Charleston, S. C.; Jenner Medical College, Chicago, 1910; died in Old Roper Hospital Sept. 22, aged 86.

Aldrich, Lewis Clarence Ⓜ Jefferson, N. H.; Maryland Medical College, Baltimore, 1902; health officer; for many years member of the school board; chairman of the board of directors of the Whitefield Savings & Trust Company; associated with the Morrison Hospital in Whitefield; died Sept. 27, aged 79.

Allen, James Henry Ⓜ Prescott, Ariz.; Georgetown University School of Medicine, Washington, D. C., 1915; fellow of the American College of Surgeons; veteran of World War I; served on the Veterans Administration Hospital in Whipple; on the staff of the Prescott Community Hospital; for many years associated with the Yavapai County Hospital, past-president of the Rotary Club; died in the Good Samaritan Hospital, Phoenix, Oct. 1, aged 72.

Ames, Charles Theron, Ipswich, Mass.; Hahnemann Medical College and Hospital of Philadelphia, 1926; died Sept. 26, aged 57.

Bacoates, Joshua Samuel, Parkersburg, W. Va.; Meharry Medical College, Nashville, Tenn., 1925; veteran of World War I; died in the Camden-Clark Memorial Hospital Sept. 28, aged 60.

Baillie, Samuel Alexander, Redlands, Calif.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1902; died in Sacramento Sept. 16, aged 85.

Baker, Sidney Franklin Ⓜ Silver City, N. M.; University of Texas School of Medicine, Galveston, 1942; past-president of the New Mexico Medical Association; member of the American Academy of General Practice; veteran of World War II; formerly associated with the Veterans Administration Hospital in Shreveport, La.; member of the staff of the New Mexico State Hospital in Las Vegas, where he died Oct. 3, aged 45.

Barfield, Hugh Howard Ⓜ Ocala, Fla.; Emory University School of Medicine, Atlanta, Ga., 1932; veteran of World War II; died Sept. 27, aged 56.

Baumbaugh, Bertha T. Patton, Santa Cruz, Calif.; University of Oregon Medical School, Portland, 1905; died Sept. 28, aged 79.

Blackshear, Thomas Joseph Jr. Ⓜ Wilson, N. C.; Atlanta (Ga.) Medical College, 1914; veteran of World War I; died Sept. 23, aged 67.

Boulet, James Irwin, Larose, La.; Tulane University School of Medicine, New Orleans, 1920; interned at the Charity Hospital of Louisiana, New Orleans; member of the school board of Lafourche Parish; at one time a member of the Lafourche Parish police jury and the parish draft board; served during World War I; member of Kappa Psi; died Oct. 2, aged 62.

Breuer, Joshua Ⓜ New York City; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1921; died in the Presbyterian Hospital Sept. 17, aged 66.

Broughton, William Edward Ⓜ Perdue Hill, Ala.; University of Louisville (Ky.) School of Medicine, 1910; served during World War I; a member of the Selective Service Board during World War II; a charter member and director of the First National Bank and a director of the Monroe County Bank; died Oct. 11, aged 70.

Burton, Edgar Curtis Ⓜ Genoa, Ill.; born in Kingston, Ill., in 1883; Northwestern University Medical School, Chicago, 1906; for a time practiced in Chicago and Craig, Colo.; past-president of the DeKalb County Medical Society; on the staff of Sycamore (Ill.) Municipal Hospital; died Oct. 12, aged 76.

Cauldwell, Earl William Ⓜ Beloit, Wis.; born in Lemont, Ill., May 10, 1916; Northwestern University Medical School, Chicago, 1944; interned at the Cook County Hospital and served a residency at the Illinois Masonic Hospital in Chicago; specialist certified by the American Board of Pathology; member of the American Association of Pathologists and Bacteriologists and the College of American Pathologists; served on the faculty of his alma mater and the University of Illinois College of Medicine in Chicago; veteran of World War II; pathologist, Beloit Hospital; died in St. Mary's Hospital in Madison Oct. 2, aged 43.

Chesmore, Harry P., St. Joseph, Mo.; Central Medical College of St. Joseph, 1900; died in the Missouri Methodist Hospital Sept. 26, aged 80.

Colley, Edward Duval, Harrisburg, Pa.; Howard University College of Medicine, Washington, D. C., 1897; died Sept. 13, aged 86.

Crumpler, Walter Emmett Jr. Ⓜ Port Arthur, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1936; veteran of World War II; died Sept. 28, aged 48.

Ⓜ Indicates Member of the American Medical Association.

Dearborn, Selwyn Kenson Ⓜ Woodsville, N. H.; born in Bristol in 1879; Dartmouth Medical School, Hanover, 1905; interned at Boston City Hospital and New York City Lying-in Hospital; practiced briefly in Lincoln; for many years was physician for the Boston and Maine Railroad; staff member of the Cottage Hospital; died Oct. 1, aged 80.

Denny, Edgar Clarence Ⓜ Milton, Ind.; Indiana University School of Medicine, Indianapolis, 1911; past-president of the Wayne County Tuberculosis Association and the Wayne County Medical Society; served on the staff of the Richmond (Ind.) State Hospital; died in the Reid Memorial Hospital, Richmond, Sept. 24, aged 75.

Dillon, Edward Saunders, Rosemont, Pa.; Harvard Medical School, Boston, 1916; interned at Children's Hospital of Philadelphia and Pennsylvania Hospital, Philadelphia; practiced in Philadelphia from 1923 until he retired in 1955; specialist certified by the American Board of Internal Medicine; at one time associate professor of diseases of metabolism, Graduate School of Medicine, University of Pennsylvania, Philadelphia; fellow of the American College of Physicians and the Philadelphia College of Physicians; president of the American Diabetes Association, 1947-1948; member of the American College of Physicians; served in the Royal British Army Medical Corps and the U. S. Army Medical Corps during World War I; at one time assistant medical director of the Penn Mutual Life Insurance Company; on the staffs of Pennsylvania and Philadelphia General hospitals and the Graduate Hospital of the University of Pennsylvania, Philadelphia; died Oct. 9, aged 69.

Dillon, James Root, San Francisco; Cooper Medical College, San Francisco, 1912; for many years professor and later head of the department of urology, Stanford University School of Medicine, San Francisco, becoming professor emeritus in 1949; charter member of the American Board of Urology; on the staffs of Stanford and St. Francis hospitals; consultant to the Santa Fe Hospital; died in Napa Oct. 5, aged 75.

Dixon, Charles Alfred, Akron, Ohio; Cleveland Medical College, Homeopathic, 1894; captain, M. C., U. S. Army, World War I; died Oct. 1, aged 88.

Fairchild, John Paul Ⓜ Freeport, Ohio; Ohio State University of Homeopathic Medicine, Columbus, 1919; died Sept. 23, aged 69.

Feingold, Samuel Jacob Ⓜ Canton, Ohio; University of Pittsburgh School of Medicine, 1914; veteran of World War I; on the courtesy staff, Mercy Hospital; died Sept. 27, aged 68.

Frew, George W. H. Ⓜ Paradise, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; for many years deputy coroner for Paradise township; served as a medical examiner for schools in Paradise and Strasburg townships; died in the Lancaster (Pa.) General Hospital Sept. 30, aged 88.

Froggatt, John Wesley Ⓜ Philadelphia; Jefferson Medical College of Philadelphia, 1925; retired medical inspector for the communicable disease control section of the city department of health; on the staffs of the Episcopal and Frankford hospitals; died Sept. 30, aged 60.

Gibson, Charles Valentine, Science Hill, Ky.; University of Louisville (Ky.) Medical Department, 1910; veteran of World War I; on the honorary staff of Somerset (Ky.) City Hospital; died in the Veterans Administration Hospital, Lexington, Sept. 27, aged 81.

Goldstein, Abraham Alvin Ⓜ Richmond Hill, N. Y.; University and Bellevue Hospital Medical College, New York City, 1918; died in the Menorah Home and Hospital in Brooklyn Sept. 28, aged 65.

Grove, Eugene H., Austin, Texas; born in Maple Grove, Minn., July 7, 1875; Northwestern University Medical School, Chicago, 1904; formerly practiced in Arlington, S. D.; also a pharmacist; died in St. David's Hospital Oct. 2, aged 84.

Hartman, Howard Russell Ⓜ Rochester, Minn.; born in Toledo, Ohio, Dec. 11, 1887; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1914; specialist certified by the American Board of Internal Medicine; member of the American Gastro-Enterological Association, International Society of Gastroenterology, Alumni Association of the Mayo Foundation, Society of the Sigma Xi, Nu Sigma Nu professional medical fraternity, and the Alpha Omega Alpha medical honor society; fellow of the American College of Physicians; in 1938 president of the section of medicine of the Pan-American Medical Association; in 1944 the president of the Republic of Colombia conferred on him the title of Officer of the Order of Boyaca of that country, and in 1940 was decorated with the Order of El Sol de Peru; an honorary member of the Academia Nacional de Medicina of Rio de Janeiro, Brazil, the Sociedad Médico-Cirúrgico del Guayaquil, Ecuador, Academia Nacionale de Medicina of Lima, Perú, Asociación Médica del Perú, and World Medical Association; appointed an instructor in medicine at the Mayo Foundation, Graduate School, University of Minnesota in 1920, subsequently becoming assistant professor, an associate professor of medicine, and emeritus associate professor of medicine; for many years head of the section of medicine at the Mayo Clinic; died in St. Mary's Hospital Oct. 6, aged 71.

Hogan, Frank Edward Ⓜ Mound City, Mo.; born in Farley, Iowa, Nov. 24, 1876; Central Medical College of St. Joseph, 1903; interned at Sisters'

Hospital, St. Joseph; member of the Holt County and Mound City welfare boards; on the staffs of the Missouri Methodist and St. Joseph hospitals in St. Joseph, and the Fairfax (Mo.) Community Hospital, where he died Sept. 26, aged 82.

Jamison, Ralph Herlinger Ⓜ Warren, Ohio; Duke University School of Medicine, Durham, N. C., 1946; interned at the Naval Hospital, Portsmouth, Va.; served a residency at the University Hospitals of Cleveland and the Veterans Administration Hospital, Cleveland; certified by the National Board of Medical Examiners in 1947; specialist certified by the American Board of Surgery; was a lieutenant (jg) in the U. S. Navy; secretary-treasurer of the Trumbull County Medical Society; on the staff of the Trumbull Memorial Hospital, where he died Oct. 5, aged 36.

Johnson, David William, Cincinnati; Tufts College Medical School, Boston, 1928; formerly practiced in White Plains, N. Y., where he was surgeon for the police and fire department; died Sept. 24, aged 59.

Kabaker, Charles Bernard Ⓜ Chicago; University of Michigan Medical School, Ann Arbor, 1938; interned at Providence Hospital, Detroit; served residencies at the U. S. Public Health Service Hospital, Lexington, Ky., University Hospital, Ann Arbor, Mich., Philadelphia General Hospital, and Hartford (Conn.) Hospital; served as a captain in the U. S. Army Medical Corps during World War I; member of the American Society of Anesthesiologists, Inc.; on the staff of St. Mary of Nazareth Hospital; died in the Veterans Administration Hospital, Cincinnati, Oct. 7, aged 48.

Kilgard, Ross Miller Ⓜ Watertown, S. D.; University of Minnesota Medical School, Minneapolis, 1932; past-president of the Watertown District Medical Association; on the staffs of the Memorial and St. Ann hospitals; died Sept. 22, aged 55.

Lanspa, Joseph Albert Ⓜ Roseburg, Ore.; University of Nebraska College of Medicine, Omaha, 1928; chief, medical service, Veterans Administration Hospital; died Sept. 28, aged 58.

Ledwin, William Joseph, Cincinnati; Eclectic Medical College, Cincinnati, 1921; for many years associated with the city health department; died Sept. 28, aged 83.

McCaffrey, Jerome A. Ⓜ Norton, Mass.; Middlesex College of Medicine and Surgery, Waltham, 1934; school physician; died Sept. 27, aged 49.

McGill, Elisha Leavenworth Ⓜ Petersburg, Va.; Columbia University College of Physicians and Surgeons, 1901; interned at Bellevue Hospital, New York City; captain in the Army Medical Corps during World War I; served as coroner of Petersburg from 1919 to 1944; on the staff of the Petersburg General Hospital; died Oct. 4, aged 84.

McGrath, Harold Francis Ⓜ Chicago; Stritch School of Medicine of Loyola University, 1931; interned at Mercy Hospital, Chicago; served a residency at the Lewis Memorial Maternity Hospital, Chicago; on the staffs of Holy Cross Hospital and Little Company of Mary Hospital, where he died Oct. 13, aged 54.

Medley, James Charles, Youngstown, Ohio; University of Pittsburgh School of Medicine, 1953; interned at the Washington (Pa.) Hospital and St. Elizabeth Hospital; served a residency at St. Joseph's Riverside Hospital, Warren, Ohio; served with the Marine Corps during World War II; died Oct. 1, aged 34.

Moore, J. Omar, Springfield, Mo.; St. Louis College of Physicians and Surgeons, 1896; died in the Springfield Baptist Hospital Sept. 24, aged 85.

Mullen, Clifford Lee, Richmond, Va.; Meharry Medical College, Nashville, Tenn., 1933; on the staff of the Richmond Community Hospital; died in the Richmond Memorial Hospital Sept. 24, aged 57.

Nelson, Holger Carl M. Ⓜ Watertown, N. Y.; Western Reserve University School of Medicine, Cleveland, 1934; interned at the Rochester (N. Y.) General Hospital, where he also served a residency; served during World War II; member of Nu Sigma Nu; on the staffs of Mercy Hospital and the House of the Good Samaritan; died Oct. 1, aged 52.

Perry, Joe Reid, Rolling Fork, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1904; died Sept. 22, aged 80.

Piantieri, Fortunato Eugene, New York City; St. Louis College of Physicians and Surgeons, 1923; died in the New York Hospital Sept. 10, aged 69.

Repass, James Chapman Ⓜ Lumberport, W. Va.; Medical College of Virginia, Richmond, 1925; interned at the St. Francis Hospital, Jersey City, N. J., and the Medical College of Virginia, Hospital Division, in Richmond, where he also served a residency; from 1926 to 1929 practiced in Raven, Va.; member of the American Academy of General Practice and Phi Chi medical fraternity; member of the Harrison County Board of Education; on the staffs of the Union Protestant Hospital, Clarksburg, and the St. Mary's Hospital, Clarksburg, where he died Oct. 5, aged 60.

Rubenstein, A. Harry Ⓜ Syracuse, N. Y.; born in Syracuse July 27, 1894; Syracuse University College of Medicine, 1919; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; professor emeritus of otolaryngology at State University of New York Upstate Medical Center; veteran of World War I; associated with the Hospital of the Good Shepherd, Syracuse Memorial Hospital, Veterans Administration Hospital, and the General Hospital; died in the Syracuse Memorial Hospital Oct. 2, aged 65.

Schimpf, Willis Henry Ⓜ Latrobe, Pa.; Georgetown University School of Medicine, Washington, D. C., 1937; interned at the McKeesport (Pa.) Hospital; served a residency at the Latrobe Hospital; past-president and treasurer of the Westmoreland County Medical Society; member of the American College of Obstetrics and Gynecology and the Latrobe Academy of Medicine; died in the Syracuse (N. Y.) Memorial Hospital Oct. 3, aged 48.

Smith, Frank Harman, Paint Lick, Ky.; University of Louisville School of Medicine, 1913; past-president of the Madison County Medical Society; former president of the Paint Lick Bank; died in the Good Samaritan Hospital, Lexington, Oct. 5, aged 76.

Suggs, Samuel David, Montgomery, Ala.; Medical Department of the University of Alabama, Mobile, 1905; died Sept. 25, aged 78.

Vollmer, Hermann Ⓜ New York City; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1920; formerly chief of pediatrics at the Augusta-Victoria Hospital, Berlin; specialist certified by the American Board of Pediatrics; assistant chief of pediatrics at the Vanderbilt Clinic of Columbia-Presbyterian Medical Center; associated with Dr. Bela Schick at the Mount Sinai Hospital, where he developed the Vollmer patch test to detect tuberculosis; on the staff of the Babies Hospital, Columbia-Presbyterian Medical Center; published many papers on pediatrics and child psychology; died Oct. 11, aged 63.

Winternitz, Milton Charles Ⓜ Washington, D. C.; born in Baltimore Feb. 9, 1885; Johns Hopkins University School of Medicine, Baltimore, 1907; fellow, assistant instructor and associate professor of pathology at his alma mater from 1907 to 1917; assistant resident pathologist at the Johns Hopkins Hospital in Baltimore from 1910 to 1913 and associate pathologist from 1913 to 1917; pathologist to the City Hospital in Baltimore from 1910 to 1917; professor of pathology and bacteriology at the Yale University School of Medicine in New Haven, Conn., from 1917 to 1925, when he became Anthony N. Brady Professor of Pathology, serving in this capacity until 1950, when he became professor emeritus; dean at Yale from 1920 to 1935; associate director of the Institute of Human Relations, Yale, from 1931 to 1950; a director of the board of scientific advisers of the Jane Coffin Childs Memorial Fund for Medical Research with headquarters at Yale; an oil portrait of him was presented to the Yale University by the student body in 1935; member of the American Society for Experimental Pathology, American Association of Pathologists and Bacteriologists, Society for Experimental Biology, National Committee for Mental Hygiene, Connecticut Birth Control League, and the Connecticut Society for Mental Hygiene; fellow of the Royal Society of Medicine and the American Association for the Advancement of Science; in 1917 was made chief of the pathology section of the medical division organized under the Bureau of Mines to study the physiological effects of war gases and to institute therapeutic measures; appointed captain in the medical reserve corps in 1918 and was placed in charge of pathology and bacteriology research at the Chemical Warfare Service Laboratory at Yale, Lakehurst, and American University; also during World War I was in charge of the laboratory division of the U. S. General Hospital in West Haven, Conn., and the division of pathology of the Yale Army Laboratory Training School; discharged from the service with the rank of major; during World War II chairman of the National Research Council Committee on Treatment of Gas Casualties; also chief of division of five of the Committee on Medical Research and chairman of its insect and rodent control committee; for his war work received the President's Certificate of Merit; chairman of the division of medical sciences, National Research Council, Washington, D. C., from 1950 to 1953; in 1932 recipient of the Newell Sill Jenkins Memorial Medal, King's Medal for Service in Cause of Freedom in 1948, and the Yale Medal in 1952; member of the board of Gaylor Farm Sanatorium in Wallingford, Conn., and the Grace-New Haven Community Hospital in New Haven, Conn.; in 1952 received an honorary doctor of laws degree from Yale University; joint author of "Biology of Arteriosclerosis"; author of "The Pathology of Influenza" and "Pathology of Vascular Disease"; compiler of "Collected Studies on the Pathology of War Gas Poisoning"; the July, 1950, issue of the *Yale Journal of Biology and Medicine* was a special number honoring him with scientific articles prepared by his associates, colleagues, and former students; died in the Hitchcock Clinic, Hanover, N. H., Oct. 3, aged 74.

Wood, Alfred Conrad, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1888; also a graduate in pharmacy; member of the American Surgical Association; American Association of Genito-urinary Surgeons, and the International Society of Surgeons; fellow of the American College of Surgeons; formerly assistant professor of surgery at his alma mater; served on the staffs of the Memorial Hospital, St. Agnes Hospital, and the Howard Hospital; wrote several books; died Oct. 2, aged 96.

FOREIGN LETTERS

AUSTRIA

Cesarean Section.—At the meeting of the Society of Physicians in Vienna on Oct. 23, Drs. V. Grünberger and F. Senker said that the indication for cesarean section had widened with the introduction of sulfonamides and antibiotics and with progress in anesthesia. A comparison of the indications and results observed at the gynecological department of the University of Vienna from 1936 to 1940 with those from 1954 to 1958 revealed that sections for pelvic contraction had decreased from 72.8 to 17.7% because of the prevention of rickets. Indications for cesarean section now include insufficiency of labor pains, primiparas of advanced age (particularly those with breech presentation), rigid os uteri, abnormal position of the infant, asphyxia of the infant, transverse presentation, prolapse of the umbilical cord, cardiac defect, tuberculosis, and Rh incompatibility. The incidence of cesarean section has been increased from 0.96 to 2.45%. The maternal death rate has been reduced from 6.8 to 1.8%.

Solution of Urate Calculi.—At the meeting of the Society of Physicians in Vienna on Oct. 30, B. Bibus reported that by chance the observation was made that large urate calculi in the renal pelvis, which might have been considered an indication for surgical removal, could frequently be dissolved by the administration of 1 or 2 lemons daily, given in the form of lemonade for several months. The success of this therapy was checked by roentgenograms. In addition to therapy with lemons, a purine-free diet was prescribed and the patient was advised to refrain from the ingestion of alcohol. A few patients were also given piperazine. This drug, however, had no demonstrable effect. In patients with chronic recurrent calculus formation in the ureters it was possible to obtain prompt relief with the lemon diet, provided the calculi were of the urate type.

Carcinoma of the Stomach.—At the meeting of the Society of Physicians in Vienna on Oct. 23, G. Poppov of Sofia stated that the definitive treatment of carcinoma of the stomach is surgical. Irradiation therapy should be avoided because of possible damage to the reticuloendothelial system in the liver and spleen. In the last three or four years the cytostatic agent, ethyleneimine quinone, was tried on 20 patients with tumors in various locations. Despite partial damage to the blood-forming system, the lives of some of these patients were prolonged by an estimated 3 to 16 months. Cytostatic treatment should, however, be combined with subtotal or total gastrectomy. Although subtotal gastrectomy is preferred by most surgeons, total gastrectomy offers better prospects for a permanent cure. This operation, however, has the disadvantage of a high operative mortality and of severe postoperative disturbances of metabolism. The primary operative mortality is due chiefly to the unreliability of the anastomosis between the esophagus and intestine and the resulting peritonitis. The disturbances of metabolism are the result of the absence of a stomach and of the exclusion of the duodenum.

The formation of a substitute stomach while the duodenum remains excluded provides for only a partial improvement of the disturbances of metabolism. On the other hand, interposition of small intestine or colon between the esophagus and duodenum leads to complaints resulting from overfilling of the duodenum. In 1950 the speaker devised an operative technique to overcome these difficulties. A substitute stomach formed from a doubled loop of the small intestine is interposed. As a result of the second peristaltic phase, which takes its course away from the pylorus, the food can be kept in this substitute stomach for a period up to four hours. Moreover, a better mixing of the food with the bile and pancreatic juice becomes possible, since the food moves through the duodenum. The most important advantages of such a substitute stomach are greater reliability of the anastomosis between esophagus and substitute stomach, avoidance of disturbances of metabolism in the postoperative period, and possibility of extending the indications for total gastrectomy.

BRAZIL

Malignant Metastases.—Dr. Antonio Prudente (*Bol. Oncol.*, August, 1959) does not believe that biopsy is a factor in the dissemination of malignant cells, since the uptake of such cells in blood vessels or lymphatics does not occur because such vessels are severed but as a result of the specific activity of the neoplastic cells which invade the capillaries. The author observed that cancer implanted into animals grew rapidly but did not show gross metastases; however, microscopic examination revealed malig-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

nant cells in the capillaries. These elements remained latent until the primary tumor was removed. The interpretation of this phenomenon may be athreptic immunity, that is, the immunity due to the absence of a nutritive process. When the primary tumor is present it absorbs all the specific nutrient substances available, but when this is removed the secondary foci are able to grow.

Auricular Septal Defects.—At the Institute of Cardiology, Sabbado D'Angelo of São Paulo, Dr. J. Medeiros (Sobrinho), and co-workers made an x-ray study of 15 patients with auricular septal defects, three of whom had an anomaly of the pulmonary veins in addition to the auricular septal defect. All patients were catheterized preoperatively and three postoperatively. Radiologic changes were studied between 1 and 12 months after operation. A correlation between the size of the defect as measured at operation and the pressure in the right auricle, right ventricle, and pulmonary artery was observed, and the radiologic findings were compared. It was observed that before operation the periphery of the lungs showed a pattern of congested vessels which in the postoperative period returned to normal. The periphery of the lung fields showed a decreased transparency on account of the greater amount of blood in comparison with the air in the alveolar spaces. The authors referred to this peculiar pattern as a "capillary veil," and its disappearance was an index of operative success.

Caudal Anesthesia for Hemorrhoidectomy.—Lemos and Schuler of Recife (*Rev. brasil. cir.* 37:278, 1959) used caudal anesthesia for hemorrhoidectomy on a series of 120 patients. These patients were divided in three groups. Group 1 (80 patients) received a 2% solution of procaine which was applied in three injections, one of 20 cc. in the sacral hiatus, and two of 5 cc., one in each of the lateral inferior orifices. In group 2 (20 patients) the same solution was used, but in a single injection of 30 to 40 cc. in the sacral hiatus. In group 3 (20 patients) a 2% solution of lidocaine was used, 20 cc. being injected in the hiatus and 5 cc. in each of the two lateral orifices.

In three patients in group 1 it was necessary to complement the anesthesia with a small amount of procaine in the perianal skin, at the beginning of the operation. The dilatation was satisfactory in all patients and no pain was reported during the operation. In nine patients of this group retention of urine was observed as a postoperative complication and eight of these had to be catheterized. In two patients in group 2, notwithstanding the good dilatation obtained and the absence of pain during the operation, it was necessary to give nitrogen monoxide by inhalation to relieve a mild pain. Three patients had retention of urine which responded to routine medication. In two patients in group 3 a small local injection of lidocaine was required at the beginning of the operation. The authors concluded that the use of 30 cc. of a 2% solution of lidocaine in three injections in the sacral hiatus and in the two lateral orifices gave the best results.

Rheumatic Fever.—Dr. Victor Schubsky and coworkers of the São Paulo State University Hospital presented to the Associação Paulista de Medicina a study of 206 patients who had rheumatic fever. Of these, 96 (46.5%) were under 13 years of age or less, 67 (32.6%) were from 13 to 20, and 43 (20.9%) were 21 or over. Polyarthritis was present in 143 (69.4%), carditis in 132 (64%), and epistaxis in 100 (48.5%). A high sedimentation rate was present in 117 (64.4%). The clinical manifestations were classified as primary and secondary. The former include (1) fever, pallor, and loss of weight; (2) arthralgia; (3) increased sedimentation rate and a positive Weltmann's serum test result; (4) upper respiratory infection; (5) epistaxis; and (6) previous history of rheumatic fever. The secondary manifestations include subcutaneous nodules and erythema. The authors concluded that the presence of two principal or of one principal and two secondary manifestations indicates a high probability of rheumatic fever.

Mycobacterium leprae.—Dr. F. P. R. Lagoa of Rio de Janeiro reported a method (*Hospital Rio de Janeiro* 56:141, 1959) of growing Mycobacterium leprae in vitro. He first washed biopsy material from human lepromatous lesions in a balanced saline solution, digested it with trypsin, shook it vigorously, and centrifuged it. Smears prepared with the sediment showed numerous acid-fast bacilli free from tissue residues. Resuspended in the saline solution and again concentrated, the sediment was inoculated in rhesus kidney cell cultures containing penicillin and a wide variety of culture mediums. There was no bacterial growth in any of the standard culture mediums, but 15 days after the inoculation, smears from these cell cultures showed the complete absence of the bacillary forms inoculated and the appearance of a cloud of fine acid-fast particles diffusely distributed.

Microscopic examinations repeated on the 25th, 30th, and 35th days showed a striking progressive transformation of the granules and cells. On the 25th day several large fuchsinophilic granules were observed in some areas of the cloud of fine particles, as well as a few renal cells which were less intensely stained and presented a central vacuole with a small fuchsinophilic granule. On the 30th day smears showed the presence of some young acid-fast bacillary forms outside of the cells and a larger number of paler cells with intravacuolar fuchsinophilic granules. On the 35th day it was possible to see a greater number of less intensely stained cells with still larger fuchsinophilic granules, some of them with an elongated, quasibacillary form, and at the same time, outside of the cells, numerous typical Myco. leprae.

The material of these cultures when reinoculated in other renal cells cultures reproduced the same progressive cycle. The bacillary forms were never seen in the interior of cells, but the infectious material was always seen in the granular form. The author concluded that in the life cycle of Myco. leprae, the intracellular granules are the young infectious elements and the extracellular bacilli are the final or adult form of the organism.

Acid-Base Equilibrium in Bronchopneumonia.—Bronchopneumonia can cause, by different mechanisms, alterations of the characteristics of the blood which vary from patient to patient, in quality as well as in intensity. Knowledge of these modifications may be used as a guide to therapy, particularly in infants. Dr. Guilherme Mattar and co-workers of the São Paulo State University studied the disturbance of the acid-base equilibrium in 17 infants with bronchopneumonia and in 10 normal controls (*Rev. paulista med.* 55:175, 1959). The authors stated that the control of bicarbonate of the plasma depends mainly on the kidneys and that of carbonic acid on the lungs. The mechanisms that cause disturbances of the acid-base equilibrium in bronchopneumonia are (1) hypoventilation due to the presence of exudate and secretions, causing difficulty in the elimination of carbonic acid; (2) hyperventilation from hyperpnea caused by fever, leading to greater loss of carbonic acid, initially by the alveoli and, afterwards, by the blood, thus inducing respiratory alkalosis; (3) dehydration determined by hydroelectrolytic losses caused by fever and by absence or diminution of the ingestion of liquids and food; (4) ketosis produced by prolonged fasting and the infection itself; and (5) such other associated factors as diarrhea and vomiting, drug intoxication, and the renal immaturity of the infant.

The biochemical study of the blood of the infants led to the following results. Five had a disturbance of the carbonic acid/bicarbonate ratio characteristic of respiratory acidosis; seven had mixed disturbances with both respiratory and metabolic acidosis; three had a pure metabolic acidosis; one had an unexplained alkalosis, perhaps due to a primary metabolic increase of the acid, compensated by elevation of the bicarbonate level; and one had a normal acid-base equilibrium. It is important to disclose the type of alteration present in each patient but this cannot be done by simple determination of the alkaline reserve because it may be increased both in metabolic and respiratory acidosis, thus making it imperative to know also the pH of the blood. Although the first need is to combat the main cause, i. e., the bronchopneumonia, it is imperative that the disturbed acid-base equilibrium be corrected.

Vascularization of the Tonsils.—The blood supply of the tonsils has an important bearing on the hemorrhages which sometimes occur after tonsillectomy. Dr. J. Mangabeira-Albernaz, of the São Paulo State University, presented a paper to the Associação Paulista de Medicína in which he explained that, adopting a topographic division of the fossula tonsillaris in 18 small sectors and registering the localization of vessels during tonsillectomy performed by careful dissection (472 under local and 228 under general anesthesia with tracheal intubation), he studied 700 pairs of tonsils. Blood vessels were found chiefly in the upper third of the fossula posteriorly. In no case was there evidence of a vascular hilum.

CANADA

Poliovirus Antibody Response.—MacLeod and co-workers studied poliovirus antibody response after various vaccination schedules in subjects of different ages (*Canad. M. A. J.* 81:443, 1959). They noted that the two first injections in the schedule produced a good response in most subjects regardless of age and that the booster dose produced antibodies to all three types in all children, even including those who had none at the beginning. The fact that satisfactory antibody levels were found 18 months after administration of the booster dose suggested that no fear need be entertained for the length of response to Salk vaccine. Two injections given with a four-week interval conferred much more immunity than one alone. The response was equally good when the second dose was given 7 to 10 months after the first. If three doses were given within a period of one month, the response was no better than if only two had been given, but if the total time interval was two months the immunity conferred was greater.

It seemed therefore that the concept of a secondary response phase beginning within four weeks and developing during the second month after the primary stimulus was correct. The authors recommended that the second dose be given not less than four weeks after the first dose and the third dose be given not less than four weeks after the second. Infants 3 to 12 months of age did not respond to the vaccine as well as older children, but the difference was not great. Most infants three months old or more respond satisfactorily to three doses of vaccine given one month apart.

Pressure on Veins and Thrombosis.—External pressure on veins has been cited as one of the causes of thrombosis. Robertson and co-workers (*Canad.*

J. Surg. 3:5, 1959) investigated the effects of direct external pressure on the wall of the inferior vena cava in a large number of adult rats. They opened the abdomen and applied a sterilized pressure foot to the surface of the vein for varying periods of time and with varying degrees of pressure. Sections of vein were removed and studied histologically at various intervals after the application of pressure. Slight pressure for a short period caused no change in the vein wall, for example with a weight of 5 Gm. applied for 10 seconds, but pressures of 10 Gm. for 30 seconds produced discrete and probably reversible lesions. When weights of 100 to 200 Gm. were applied for one to three hours, there was definite destruction of endothelium and a small thrombus formed at the pressure site. Repair was sometimes observed by proliferation of endothelial cells at the edges of the lesion. The authors suggested that some cases of thrombophlebitis in man may be traced to the effects of direct pressure on veins after sitting in a cramped position, and it is possible that as a result of these unnoticed injuries the process of endothelial damage, thrombosis, and repair is constantly taking place in various parts of the body.

Quadruple Immunization.—Wilson and co-workers (*Canad. M. A. J.* 81:450, 1959), using a stable quadruple antigen (diphtheria toxoid, pertussis vaccine, tetanus toxoid, and poliomyelitis vaccine), found that its potency showed no loss over a period of 14 months when stored at a temperature of 4 C. In a clinical trial the multiple vaccine had been stored for 8 months when the first dose and 10 months when the last dose was given. In this trial, 51 infants were given three doses of the vaccine while 8 controls received poliomyelitis vaccine alone from the lot used in preparation of the mixture. Each vaccine was given in three doses at intervals of four weeks; 0.5 ml. was used for the first dose and 1 ml. for the next two doses in infants under 6 months and three doses of 1 ml. each for those over 6 months of age. Blood was sampled before immunization and 14 days after the third dose for antibody to the three types of poliovirus and for diphtheria and tetanus antitoxin titers. Agglutination studies for Hemophilus pertussis were incomplete.

The response of infants to the three doses, followed by a fourth dose 12 months after the primary series, was highly satisfactory; 85% reponded to type 1 poliovirus and over 90% to types 2 and 3; and 100% responded well to diphtheria and tetanus immunization. The recommended age of immunization was determined by the desire to achieve immunity to whooping cough as early as possible. At 3 months of age, 30 to 50% of infants had maternal antibody to both poliomyelitis and diphtheria. This made it difficult to determine the proportion of postvaccination antibody due to the vaccine and that due to the mother. The fourth dose given 12 months after the course elicited the recall type of response and established a sound immunity. It was suggested that the first dose of the combined vaccine should not be reduced in infants under 6 months of age, in order not to diminish the volume of type 1 poliomyelitis vaccine component.

CHILE

Corticosteroids for Nephritis.—Dr. G. Stegen studied a series of 51 children with acute nephritis. A control group of 25 were treated with bed rest, diet, penicillin, hydralazine, and digitalis. The remaining 26 received, in addition, 1 mg. per kilogram of body weight of prednisone daily for 10 days. A striking improvement was observed in the second group as compared with the controls. No side-effects were observed and the time of hospitalization was significantly lower than that of the control group. The only death that occurred was in the control group.

Obstructive Laryngitis.—An epidemic of obstructive laryngitis in children occurred in 1958. Dr. E. Cassorla and co-workers (*Rev. Chil. Pediat.* 30:121, 1959) studied a series of 216 such patients and found that the morbidity was higher in the group aged one to two years. Malnutrition was observed in 71.5%. Pulmonary complications were more frequent when the laryngitis was associated with measles. Tracheotomy was performed in 19.3%. The case fatality rate was 11.5%. A pathological study of 46 cases revealed that the most frequent complication was bronchopneumonia, which was the cause of death in 60.9% of those who died. Status thymicolymphaticus was found in the 43.5% of the cases.

DENMARK

Serum Glutamic Oxalacetic Transaminase Activity.—Pronounced elevations of serum glutamic oxalacetic transaminase (SGO-T) activity were found in some patients with acute cardiac insufficiency without evidence of myocardial infarction, and in some with acute myocardial infarction excessively high SGO-T values were observed amounting to about eight times the usual elevations. These findings raised the question of whether damage to an organ other than the heart muscle could have been responsible for these pronounced elevations of SGO-T. Attention was focused on the liver, since this organ is known to be sensitive to acute circulatory failure. Furthermore, the liver contains large amounts of glutamic oxalacetic transaminase. N. U. Bang and co-workers (*Acta med. scandinav.* 164:385-393, 1959) examined 31 patients (13 with acute myocardial infarction, 10 with cardiac insufficiency, and 8 without cardiac disease). SGO-T values measured daily during hospitalization were compared to the postmortem histological liver findings. Microscopic evidence of centrilobular liver cell necrosis was found in all specimens from patients with pronounced elevations of SGO-T except one, and a rough correlation between the degree of centrilobular liver cell necrosis and SGO-T elevations was noted.

In two patients whose transaminase values were elevated several weeks prior to death, the postmortem specimens showed evidence of centrilobular liver cell necrosis in the process of healing, resembling that seen in incipient cirrhosis of cardiac origin. The hypothesis was proposed that centrilobular liver cell necrosis might stimulate the development of the cardiac type of cirrhosis. These observations suggested that an extracardial factor played a significant role in the production of the SGO-T elevation after acute myocardial infarction. Probably the acute cardiovascular insufficiency resulting from the myocardial infarction led to acute circulatory damage of the liver, resulting in release of enzymes into the blood stream. No consistent relationship between shock or auricular fibrillation and the presence of centrilobular liver cell necrosis could be demonstrated.

The authors postulated that centrilobular liver cell necrosis was the result of an acute episode of right heart failure in the presence of chronic cardiac insufficiency. They also suggested from their observations that acute episodes of right heart failure in the presence of long-standing chronic hepatic congestion might play a major role in the development of the cardiac type of cirrhosis. They commented that in the SGO-T test they might have found a tool with which subclinical episodes of liver damage leading to the formation of the cardiac type of cirrhosis could be demonstrated in vivo. Their results also demonstrated the serious limitations of the SGO-T test in patients with acute heart failure. In such patients in whom the presence of an underlying myocardial infarction frequently could not be demonstrated by means of the routine laboratory methods, the SGO-T test had been claimed to be of value, but the authors concluded that an elevated SGO-T activity in a patient with acute heart failure must be interpreted with caution and that it did not necessarily indicate the presence of myocardial infarction.

Postoperative Renal Function.—Ebbe Kragelund (*Acta chir. scandinav.* 117:416-426, 1959) demonstrated, on the basis of postoperative studies of creatinine clearance in 68 patients who had undergone major operations, that changes in the renal function developed in 45 of the patients. The series must be regarded as selected, as the patients seeking medical aid at the department of surgery of the Finsen Institute in Copenhagen were predominantly over 50 years of age. In 44 of the patients the operations were for malignant diseases of the esophagus, stomach, pancreas, colon, or internal female genitalia. Sixty-one of the patients had diminished or normal urinary excretion of creatinine during the first 24 hours after operation. The impairment of the renal function seemed to be directly related to the severity of the operative trauma and showed the highest incidence in older men with arteriosclerosis who had had a large blood loss and a drop in blood pressure on the day of operation. With regard to the prognosis the primary operative mortality was 3%, or two deaths. The author concluded that postoperative determinations of the serum creatinine concentration alone might be misleading, because changes in the tissue production of creatinine due to metabolic factors exerted a greater influence on the serum creatinine level than did the change in the renal creatinine excretion due to possible hemodynamic factors.

FINLAND

Eosinophilic Pleural Effusion.—Information regarding the prognosis of eosinophilic pleurisy is scanty. Even in patients with a good primary cure the tuberculous basis of this disease may become manifest later. Järvinen and Kahanpää (*Acta med. scandinav.* 164:245-251, 1959) investigated long-term results in 17 patients with eosinophilic pleurisy, either idiopathic or associated with a transitory pulmonary infiltration. The degree of pleural eosinophilia varied from 11 to 70%. The pleural exudate of 10 patients contained blood. Simultaneous eosinophilia of the blood was found in 10 patients. The cure in patients with eosinophilic pleurisy was generally more rapid, even in the absence of specific therapy, than that usually obtained in patients with idiopathic exudative pleurisy. The average duration of hospitalization was 43 days.

To determine the long-term results in patients with eosinophilic pleurisy, follow-up examinations were made 5 to 12 years after the onset of the disease. Two patients had developed pulmonary tuberculosis. This morbidity must be considered low compared with that of patients with idiopathic exudative pleurisy. A control study showed that pulmonary tuberculosis developed in 21 of 52 such patients, or 40%. Pleurisy recurred in two of the patients with eosinophilic pleurisy. The results of the investigation suggested that eosinophilic pleurisy was fairly strongly sex-linked, as 15 of the 17 patients were male. There was an antecedent respiratory infection in 10. Four patients had a coincidental peptic ulcer. Bronchial asthma appeared later in two patients. The prognosis appeared to be good and primary recovery was more rapid than in patients with ordinary exudative pleurisy. The fact that the pleural exudate contained blood in 10 of the 17 patients studied often causes the clinician erroneously to suspect malignant neoplasms or pulmonary infarction.

Pernicious Anemia and Gastric Carcinoma.—A series of 69 patients (13 men and 56 women) with pernicious anemia was studied by M. Siurala and co-workers. (*Acta med. scandinav.* 164:431-436, 1959). The mean age of the patients was 66.7 years. A control series consisting of 405 patients with a mean age of 66.0 years was studied; 29 patients had gastric carcinomas; 963 relatives of 60 patients had pernicious anemia; and 911 relatives of 54 successive patients did not have pernicious anemia. The incidence of carcinoma in the patients with pernicious anemia was 7.5% (9.8% in those over 60 years of age). This incidence was significantly higher than that for carcinoma in the total population. It was also significantly higher than the incidence of gastric carcinoma (3.0%) in patients admitted for x-ray examination of the stomach in the same period and same outpatient department. Benign polyps were present in 6.0% of those with pernicious anemia and in 1.2% of the controls; 12 of the relatives of the patients with and only 4 of the relatives of the patients without pernicious anemia had carcinoma. The mean duration of pernicious anemia was more than twice as long in those with than in those without carcinoma, but the authors warned that the material was too limited to warrant any definite conclusions on this point.

In view of the high incidence of carcinoma in patients with pernicious anemia, it seemed reasonable to conclude that patients with pernicious anemia, especially those above 60 years of age, should have regular roentgenologic examinations. Histological examination of mucosal biopsy specimens from these patients all revealed atrophic changes with some kind of metaplasia. Recent studies with radioactive vitamin B_{12} seemed to support the view that atrophic changes of the gastric mucosa were responsible for the absence of intrinsic factor leading to pernicious anemia. On the other hand atrophic changes of the gastric mucosa occurred in most patients with carcinoma. Most gastric carcinomas appeared to originate from atrophic gastritis, particularly from the areas of intestinal metaplasia which were commonly encountered in the gastric mucosa of such patients. From these findings it would appear that atrophic gastritis was the connecting link between gastric carcinoma and pernicious anemia.

Hereditary Intestinal Polyposis.—Hereditary intestinal polyposis is a rare familial disease associated with melanin pigmentation of the lips, buccal mucosa, and facial skin. Aarne Rintala (*Acta chir. scandinav.* 117:366-373, 1959) stated that little has been written on the histology of the polyps in this disease. In almost all of more than 100 reported cases polyps were present in the small intestine. In about 50% of the patients polyps were found also in the region of the large intestine, including the appendix and rectum, while only 25% had gastric polyps. The author removed polyps from three patients, a father and two daughters. The appearance of bands of smooth muscle among the glandular structures of the polyps has been erroneously interpreted as invasion, but true malignant degeneration was rare and metastases have never been found. The author concluded that the probability of the development of malignancy in patients with this disease was definitely less than in those with polyposis of the colon. Radical resections should be avoided and surgical treatment should be limited to excision of the polyps.

Varicose Veins.—Erkki Saarenmaa (*Acta. chir. scandinav.*, vol. 117, supp. 241, 1959) stated that true cavernous hemangiomas of the lower limb were sometimes difficult to distinguish from varicosities and that the difference might be only theoretical. The treatment was most adequate when an attempt was made to destroy the varicosis as completely as possible. The author believed that varicose veins should be treated at intervals as is the case with carious teeth. For the diagnosis of varicosis the functional tests (Trendelenburg, etc.) were of little importance, but the clinical features and retrograde phlebography supplemented each other in the presence of valvular incompetence of the deep veins. Retrograde femoroiliac phlebography was not capable of furnishing conclusive information if the valves proximal to the popliteal vein were competent or in the presence of total postthrombotic occlusion of the deep veins proximal to the popliteal vein.

As regarded therapy in the presence of simple primary essential varicosities or insufficiency of the superficial veins, sclerosing injections were widely used; combined with high ligature of the long or short saphenous vein and effective compression, this method offered a means of obliterating both peripheral and proximal varicosities. In the presence of superficial venous insufficiency, even when associated with deep venous insufficiency caused by complete postthrombotic occlusion or congenital atresia, therapy was directed to obliteration of the peripheral portions of the superficial varicosis. A sclerosing treatment was used combined with continued compression treatment and radical removal of leg ulcers and skin grafts.

In the presence of insufficiency of the deep venous system as a result of recanalization after deep thrombosis, the author suggested segmental resection at different levels. This tends to obviate the deleterious effect of the hydrostatic pressure of the blood column and of popliteal insufficiency on the superficial veins and capillaries and to link the blood flow in the collateral capsular and muscular networks. Resection of the popliteal vein as therapy for the varicotic syndrome was beneficial even when the deep venous system proximal to the popliteal fossa was totally occluded (postthrombotic occlusion) or when it was fully patent without valvular incompetence. The author concluded that as yet no method has been evolved which was capable of preventing recurrence and that conventional forms of therapy in the superficial network tended to induce varicotic lesions in distal but intact tributaries.

Arterial Circulatory Insufficiency.—Björn L. Lindström (*Acta chir. scandinav.*, vol. 117, supp. 242, 1959) tested the peripheral cutaneous circulation and its correlation with muscular circulation in patients with obstructive arterial disease in the legs. A bicycle ergometer was used, and the skin temperature reaction of the legs after pedaling in a sitting posture was observed in 8 healthy subjects and 25 patients with peripheral arterial disease. Muscular work by four healthy subjects before exposure of the lower limbs for one hour to a temperature of about 20 C was followed by a marked rise in skin temperature of the feet, but this skin temperature reaction failed to appear in connection with the same amount of work after the exposure. After exposure of the extremities to room temperature, moderate exercise was performed in three sessions with a 10-minute working phase alternating with a 10-minute rest period with the subject in a horizontal position. A positive skin temperature reaction in the feet was obtained in only one of four healthy subjects.

For determination of the peripheral skin temperature response after pedaling and its potential value for evaluating the peripheral circulatory insufficiency, 25 patients with peripheral arterial disease in the lower limbs were subjected to serial exercises without preceding exposure to room temperature; it was observed that the skin temperature reaction depended on the peripheral vasoconstrictor tone. Of 50 limbs investigated 66% exhibited a positive skin temperature response. Thus the skin temperature reaction depended on the vasoconstrictor tone; and therefore the circulatory insufficiency could not be judged on the basis of the peripheral skin temperature response after exercise.

Ischemia was noticed in 13 of 14 limbs with peripheral obstructive arterial disease in connection with exercise with elevation of the limbs, while only three became ischemic and five cyanotic when the subject was pedaling in a sitting posture. Arteriography was performed on 60 limbs, of which 57 had manifest arterial changes. The author divided his series into an aortoiliac, a femoropopliteal, and a distal group after the localization of the most proximally noticeable arterial changes. The symptoms of insufficiency of the cutaneous circulation were, on the average, most pronounced in patients with changes in the abdominal aorta and the iliac arteries. With the exception of patients with a strong peripheral vasoconstriction associated with the arterial disease, there was a correlation between an increasing duration of the ischemic phase and an increasing degree of severity of the arterial changes. In the sympathectomized limbs only patients with arterial changes showed correlation of the findings of insufficiency of the cutaneous circulation furnished by the function test. The insufficiency in the cutaneous and muscular circulation mutally displayed great variations; the muscular capacity would be satisfactory while the cutaneous circulation was poor, and vice versa. The author emphasized the need for a function test to aid in following the development of peripheral arterial insufficiency. The function test described made possible an objective assessment of the peripheral symptoms of insufficiency originating in peripheral arterial disease.

FRANCE

Iproniazid in Psychiatric Therapy.—Insua and Berard, (*Presse méd.* 67:1458, 1959) treated, with iproniazid, 77 patients who had depression (endogenous, involutional, symptomatic, psychogenic, and reactive), 4 who had dementia or schizophrenia, 2 who had hallucinatory or delusional psychoses, and 17 who had obsessional neurosis. The drug was effective in small doses (25 to 100 mg. per day), was well tolerated, and gave excellent results on the whole as an antidepressive agent and as a drug for the symptomatic treatment of obsessional neurosis. It was especially useful in the treatment of symptomatic depression.

Ethienomide for Tuberculosis.—Paul Veran and co-workers (*Presse méd.* 67:1597, 1959) found that ethienomide had an antibacillary activity against Mycobacterium tuberculosis between that of isoniazid and that of streptomycin. It may be given with isoniazid in patients with new tuberculosis or to replace it in treating infection with resistant organisms. It may cure long-standing lesions refractory to the usual antituberculosis drugs. Ethienomide may irritate the digestive tract, but this is less likely when it is given in suppositories.

H. Joly and J. P. Scherding (*Presse méd.* 67:1600, 1959) used the same drug for more than one year in treating more than 150 patients with pulmonary tuberculosis. Ethienomide is of value in the preoperative treatment of patients in whom the usual bacteriostatics have lost their efficiency. It may also be used locally for the treatment of tuberculous cavities or wounds. This local action of the new drug was superior to that of all other antituberculosis drugs. In 46 patients subjected to phrenic exeresis and in 8 who had surgical collapse, 0.75 to 1.0 Gm. of the drug was given daily along with other antituberculosis drugs. No major complications were noted in the postoperative course of these patients.

Glaucarubine for Amebiasis.—C. Pedoya and co-workers (*Presse méd.* 67:1481, 1959) treated 10 patients who had intestinal amebiasis with glaucarubine, a crystalline glucoside of Simarouba glauca. They gave 175 to 200 mg. of the drug daily by mouth for five to seven consecutive days. The results were excellent and the drug was well tolerated.

Portocaval Encephalopathy.—F. Contamin (*Presse méd.* 67:1607, 1959) said that neuropsychiatric troubles of hepatic orgin are not, primarily, due to a serious liver insufficiency and that coma is a major indication of this state. Less serious effects, which are reversible, may be the result of the collateral portocaval circulation which, as it traverses the liver, releases part of the venous blood coming from the intestine. The effects of greatest importance are disorders of consciousness, trembling, and electroencephalographic changes. They are caused by the presence of nitrogenous substances of alimentary, pharmacological, or hemorrhagic origin in the intestinal lumen where they undergo bacterial disintegration. Most of the clinical, experimental, and biochemical tests indicate ammonia to be the chief nitrogenous substance. Diagnosis of portocaval encephalopathy is of more than mere theoretical interest. Appropriate dietetic and therapeutic measures can prevent recurrence.

Control of Anticoagulant Treatment.—M. Mouquin and co-workers (*Presse méd.* 67:1629, 1959) devised a method for controlling treatment with coumarin derivatives. The heparin tolerance test, through its many sources of error, loses much of its value; thromboelastography, although more exact and reliable, can hardly become a routine procedure. The proposed technique is simple and precise, is based on modern measurement of coagulation time, with use of silicone-treated tubes, and should be practiced systematically and in association with the Quick method.

Ovarian Cysts.—J. C. Reymond and co-workers (*Presse méd.* 67:1637, 1959) noted the appearance of large hyperacute ovarian cysts occurring shortly after intramuscular injections of gonadotropic hormones. Such a treatment had been instituted in a 35-year-old woman with amenorrhea and secondary sterility. It as given also to a 16-year-old girl in order to promote the menarche. The first patient had received 5,000 I. U. of serum gonadotropin and 10,000 I. U. of chorionic gonadotropin, and the second received three injections of chorionic gonadotropin. Prior to this treatment the ovaries were of normal size in both patients. However, 10 and 14 days, respectively, after the first injection both had to be operated on because of the rupture of enormous, bilateral, and symmetrical ovarian cysts.

GERMANY

Mitral Stenosis Treated Conservatively.—Zapfe and Nehls (*Arztl. Wchnschr.*, vol. 14, 1959) found evidence of rheumatic disease of the mitral valve in 273, or about 3%, of 8,563 autopsies. Rheumatic disease of the other valves was taken into account only if there was a coincident involvement of the mitral valve. The average age at death for this series was 64.1 years. Even for those with severe stenosis it was only a little under 60. A combination of valvular defects—mostly mitral and aortic—was associated with a reduced expectation of life. For those who had had severe stenosis the degree of loss of function for each person at different ages and the duration of obvious cardiac decompensation were ascertained. These facts were of particular interest in the cases of patients who had survived beyond the age of 60. Among these there were only three who had showed any significant loss of function for more than five years, while among those who died before the age of 60 the duration of incapacity averaged seven and one-half years.

Rheumatic heart disease in the absence of any valvular lesion of note was rarely a cause of death, but with increasing severity of valvular involvement rheumatic disease was more often the cause of death. Fresh verrucous vegetations were found in 52, but some of these patients had died from extracardiac causes and the activity of the rheumatic process could not always be judged with certainty. Over 50% of the patients with a positive history of rheumatic fever had had their first attack before the age of 20 and nearly 75% before the age of 30. Since the remaining 25% remained clinically silent, the percentage of unrecognized mitral stenosis increased in proportion to the age at death. Failure to recognize mitral stenosis was probably due in many cases to concomitant hypertension, which was present in 23.8% but was rarest among those with severe mitral stenosis. Only one of the 10 persons with mitral incompetence had had hypertension. In almost every case the hypertension was of the essential type.

The most interesting result of this investigation was the unexpectedly high average age at death for patients who had had mitral stenosis of all grades of severity. It was also significant that a group of long-lived patients who had had severe stenosis seemed to have been severely incapacitated only a short time when compared with those who died at an earlier age. This may mean either that only small demands had been made on their physical capacity during life, that a valvular lesion which was initially trivial became serious only in later years, or that the first attack of rheumatic fever may have occurred at a comparatively advanced age. Aggravation of stenosis by calcification in old age no doubt also plays a part in this matter. According to these data the question of operation at an earlier age would arise only for those with severe stenoses, in whom a serious loss of function had been present before the age of 50. Apart from this group, however, there are many persons with mitral stenosis who have a good expectation of life even without operation and who retain a good exercise tolerance for many years.

Third Stage Pains, Placental Separation, and Hemorrhage.—Puder and Klein (*Deutsche med. Wchnschr.*, vol. 84, 1959) stated that a few seconds or minutes after the birth of a child the tone of the uterus increases and reaches its maximum after separation and delivery of the placenta. Occasionally this increase in tone is absent without postpartum hemorrhage resulting, and conversely hemorrhage may occur when the uterine tone is perfectly normal. The significance of the pains or the increased uterine tone in the third stage of labor in relation to placental separation and blood loss is still undetermined, but they suggest a disturbance of the mechanism of coagulation. For this reason some sort of oxytocic preparation is usually given after the birth of the head or just after the end of the second stage, in the belief that conditions for the third stage are thereby improved.

This belief was tested in 6,625 deliveries. From these it was clear that any increase in the third stage pains brought about by drugs or any other means had an unfavorable effect on placental separation and hemostasis. It seems, therefore, that other factors are decisive in this matter. Undoubtedly the degree of maturity of the placenta is important. With increasing maturity the fibrinous deposits increase and the thromboplastin content decreases. At the same time coagulation necrosis occurs in the decidua. When separation takes place the thromboplastin is used up.

These investigations showed that the physiological mechanisms of coagulation play a more important part in placental separation than do the mechanical forces hitherto held responsible. During separation the fibrin deposits in the basal layer and intervillous spaces are increased by the activation of the placental thromboplastin, which also causes increased coagulation in the maternal vessels. Thus, hemorrhage should be possible only retrogradely from the intervillous spaces. Once the maternal blood has flowed away the fetal blood can find its way into the villi. The umbilical cord, which up until then has been tense and full, collapses, and this can be taken as a sign of separation. Stagnation of the maternal blood in the placenta, which takes place after the child's first cry, triggers the resolution of the fibrinous layer via the activation of thromboplastin. Uterine contractions may sometimes compensate for a slight degree of placental insufficiency, but they are not absolutely necessary for hemostasis when placental function is fully intact.

Trichomoniasis.—H. J. Keutel of Dresden (*Hautarzt*, vol. 10, 1959) stated that in trichomoniasis the diagnosis depends primarily on the demonstration of trichomonads in smears from vagina, cervix, urethra, prepuce, or seminal fluid, which must be examined when they are as fresh as possible. The chief feature which distinguishes the organism from other cells is its mobility and motility. With vital staining the number of organisms seen is usually much greater than in fresh smears. The authors showed from an examination of sexual partners that in 97% of 86 pairs, both members were harboring trichomonads. In a series of men with trichomoniasis, most complained of prostatic symptoms. Only 18.7% were symptom-free. Most of those with symptoms had a chronic prostatitis, often combined with vesiculitis, urethritis, or epididymitis. In women the parasite generally gave rise to burning sensations and itching, loss of sleep, loss of weight, and anxiety about venereal disease. Not uncommonly the inflammation of the introitus produced a form of vaginismus.

Since the infection is generally chronic in both parties, treatment requires great patience. Success can only be achieved by combining local and general treatment. Total sexual abstinence for six to eight weeks is a precondition of success in treatment. The most effective local measures in the female consist of vaginal douches with disinfectants and the insertion of vaginal tablets. Peter and Jirovec recommended giving hormones to encourage proliferation of the vaginal epithelium. A combination of these measures with sulfonamides to control the associated bacterial flora has given good results. Marked subjective or objective improvement should under no circumstances prevent the continuation of treatment, which for the first three weeks is best carried out by the doctor. Pregnancy is no contraindication to treatment. Indeed, it makes disinfection of the vagina even more desirable.

In general, treatment should last between two and three months. In postmenopausal women tablets should be inserted in the vagina for six months, since in this period of life recurrences are very likely. Trichomoniasis of the bladder can be successfully treated with instillation of Tricofuron, which is also suitable for local treatment of vaginal infection. As a general measure the author used Rhodoforman and also considered the use of neoarsphenamine. The poor circulation in the prostate renders treatment more difficult in the male and fever therapy may be necessary for complete success. Mud baths or local diathermy may be helpful. The author found that local treatment combined with an intensive course of quinacrine, even to the point of producing yellowing of the skin, plus antibiotic treatment to control the associated bacterial flora, was an effective method of treatment.

Radioactive Gold in Gynecology.—D. Hofmann of Giessen (*Ther. Gegenwart*, vol. 98, 1959) stated that the advantages of the artificial radioactive isotope Au^{188} consist partly in the fact that it has a half-life of 2.7 days, which means that after 10 days its activity has fallen to less than 10% of the initial value and partly in the fact that 95% of its radioactivity is in the form of electrons with a maximal energy of 0.96 MeV and 5% is in the form of gamma radiations with a maximal energy of 0.41 MeV. The latter fact permits the easy detection of the presence or distribution of the isotope by means of a Geiger counter. Measures for protection against radiation are greatly facilitated by these properties. In particular Au^{188} can be left in the patient's tissues since its radioactivity is soon virtually exhausted. The beta radiations penetrate to a depth of about 2 mm. while the gamma rays reach practically all organs. The colloidal form in which Au^{188} is generally used in gynecology ensures that it remains at the site of injection and is not carried away to any significant extent in the lymphatics.

In gynecological practice Au^{188} is usually given intraperitoneally or intrapleurally. The author used it for almost all stages of metastasizing tumors in the abdominal or thoracic cavities, in some patients in combination with radium or x-ray. In patients with stage 1 ovarian carcinoma the abdominal cavity was irradiated with Au^{188} alone after radical oophorectomy; 200 to 300 cc. of saline solution were first injected into the abdominal cavity, then the gold suspension was given after the withdrawal of only so much ascitic fluid as would allow proper dilution of the Au^{188}. When the substance was given intrapleurally or intraperitoneally it rapidly became adsorbed on the serosa of the cavity and was slowly carried away in the mediastinal or mesenteric lymph vessels. The greater part of the radioactivity found its way eventually to the liver and spleen, as it did after intravenous injection. In practice it was impossible to calculate the exact dosage of Au^{188}. Clinically doses were determined empirically. As a routine the author gave two doses of 100 mc. at an interval of about four weeks. For peritoneal pseudomyxoma he gave two doses of 150 mc. Apart from its intracavitary application 80 to 100 mc. of colloidal Au^{188} was also given intratumorally to patients in whom there were metastases to the inguinal glands.

The author achieved striking palliative results by applying Au^{188} at laparotomy to residual infiltrations from ovarian carcinoma and also to carcinomatous pleurisy with effusion, in which condition recurrences generally did not appear after the second application. Results with ascites were not so encouraging. In patients who had lymphatic metastasis, however, especially with carcinoma of the vulva or urethra, intratumoral injection of Au^{188} had no effect on the course of the disease even when the local results were promising. In all events inguinal injection of Au^{188} was often followed by unusually diffuse metastasis in the skin of that region. On the other hand, in three patients with peritoneal pseudomyxoma freedom from recurrences for periods up to two years was obtained. Postoperative irradiation of patients with groups 2 and 3 ovarian carcinomas gave definite palliation. The survival rate was greater in the treated cases. Side-effects of Au^{188} treatment by the intravenous route consisted in damage to liver, spleen, and marrow, whereas when the gold was given intracavitarily or intratumorally there was generally no significant effect on the reticuloendothelial system. General effects of radiation such as disturbance of liver function are not to be expected, but as with radium and x-ray treatment, systemic upset in the form of radiation sickness does occur—generally to a lesser degree than after x-ray therapy.

Serum Potassium and Sodium in Liver Disease.—Hennrich and Breuer of Bonn (*Arztl. Wchnschr.*, vol. 14, 1959) investigated the serum electrolyte levels in 13 patients with uncompensated and in 37 with compensated cirrhosis of the liver. All patients in the first group showed various signs of parenchymatous failure in addition to more or less marked ascites. Values for serum sodium were in the range of normal with a slight tendency to subnormality. The values for potassium were normal in some, raised in some, and decreased in others. The mean value of 22 estimations was 4.63 mEq per liter, somewhat lower than the normal value for healthy subjects (4.8 mEq per liter). Only four values were below the normal range. There was no relation between the serum electrolyte values and the results of the liver function tests.

About 43% of the patients with compensated cirrhosis tended to hypokalemia, 21% tended to hyperkalemia, and the rest had fluctuating values, while the values for serum sodium levels were all within normal limits. All these patients showed a balanced water-metabolism. In this group, too, there was no direct relation between the serum electrolyte concentration and the extent of the liver damage. A disturbance of potassium metabolism, in particular in the direction of hypokalemia, in patients with liver disease might be attributed to the following factors: reduced potassium intake after anorexia or complete starvation in comatose patients; increased protein breakdown and negative nitrogen balance, which leads to diffusion of potassium out of the liver cells; damaged liver function resulting in inability on the part of the cells to store potassium against the concentration gradient; increased glycogenolysis, whereby potassium is released; decreased inactivation of posterior pituitary antidiuretic hormone due to liver damage; increased corticosteroid formation as a result of general stress; and loss of potassium due to diuretic treatment.

The authors observed a tendency to hypokalemia in most of their patients but did not find any evidence of a relationship between hypokalemia and hypoproteinemia. In those with hypokalemia and liver damage the potassium metabolism must be adjusted so that enough potassium is available for the increased protein synthesis and glycogenesis. Even with a prolonged negative potassium-balance a normal serum potassium level may be maintained for a long time and a latent hypokalemia may be masked by dehydration, for instance, so that the actual values may be normal, or even raised. Because of the numerous causes of a disturbed potassium metabolism, views regarding the level of serum potassium in liver disease differ widely. The authors found that in three patients on whom a portocaval anastomosis had been performed the serum potassium was first raised and then definitely reduced. The hypokalemia which is almost always found after operations was undoubtedly accentuated here by the increased protein loss, which was particularly marked in the presence of hepatic cirrhosis and the consequent metabolic disturbance. To prevent this postoperative hypokalemia, which often results in paralytic ileus or atony of the stomach or bladder and not uncommonly in clouding of consciousness or coma, continuous replacement of potassium is necessary.

New Steroid Derivatives in the Treatment of Tumors.—L. Zicha of Erlangen (*Therapiewoche* 9:512, 1958/1959) treated 10 patients who had mammary carcinoma, 2 who had carcinoma of the thyroid, 2 who had carcinoma of the head of the pancreas, and 1 who had melanosarcoma with a fluorated testosterone derivative, Ultranden, for one to four months. They also treated patients who had carcinoma of the breast, with a bromine derivative of progesterone, Broxoron, for two to three months. With this treatment the sedimentation rate, alkaline phosphatase level, and plasma protein level all showed a distinct tendency to return to normal. No significant regression of radiologically visible metastases was observed within a maximum period of observation of four months. With both substances a slight rise in blood pressure was occasionally noted.

Ultranden had no detectable influence on mineral metabolism, but a potassium deficiency was observed after four to six weeks in patients taking Broxoron. Virilization did not occur with either of the preparations. Suppression of adrenal cortical function, as measured by the excretion of 17-ketosteroids and 17-ketogenic steroids, before and after administration of ACTH, did not occur. Two women treated with Ultranden and one treated with Broxoron were able to do their housework again after three months' treatment, when previously they had had to have a nurse. Doses of 40 mg. of Ultranden were equivalent to about 10 times that amount of Broxoron. While Ultranden could be used in general practice, with Broxoron it is advisable to have clinical controls.

UNITED KINGDOM

The Criminally Insane.—Treatment of a series of 100 dangerously insane patients with chlorpromazine, prochlorperazine, and pentazine has achieved encouraging results, according to the Board of Control's report for 1958. The board believes that the most encouraging trend is that the necessity to use compulsory powers under the Lunacy and Mental Treatment Acts is diminishing. This was reflected in the rise in voluntary admissions to the highest figure, or 85% of total admissions so far. Readmissions represented 44.8% of the total admissions in 1958. Although the total number of persons admitted continued to increase, the number in the hospital at any one time declined steadily. This suggested that more effective treatment was enabling accommodation to be used more efficiently, thus reducing the average length of stay.

Surgical Relief of Myocardial Ischemia.—In the past 30 years various surgical measures have been introduced to increase the blood supply to the ischemic myocardium. The object has been to develop a collateral circulation to counteract the effects of coronary atherosclerosis by abrasion of the parietal pericardium and epicardium or by the introduction of irritants into the pericardial sac. Sir Russell Brock and co-workers (*Lancet* 2:631, 1959) stated that they found no satisfactory evidence that such operations were effective. They believed that operations designed to improve the intercoronary anastomoses and produce a more favorable distribution of blood within the myocardium were more rational. They abraded the parietal and visceral pericardium to try to produce a myocardial reaction sufficiently brisk to improve the intercoronary anastomoses in a series of 10 patients with severe angina pectoris treated in this way. All had progressive and incapacitating angina that was not relieved by medical treatment. They had no cardiac enlargement, cardiac failure, severe hypertension, or generalized arterial disease.

The exercise tolerance was assessed before and after operation by a standard test, and a 12-lead electrocardiogram (ECG) was taken before and after the exercise. Under supervision the patient was encouraged to continue exercise until pain, dyspnea, or fatigue were produced and the symptoms were recorded. This assessment was made two, four, and six months postoperatively. The number of attacks of pain before and after operation was also noted. The patients were digitalized before operation and throughout the immediate postoperative period. The results, after six months, were excellent in three patients. One of them was working full time and was free from anginal symptoms with normal activity when last seen. Ten-minute exercises failed to produce pain in this patient. The condition of two other patients improved strikingly, while the results were classed as good in five others. In one patient improvement was slight. The ECGs correlated with the postoperative clinical findings. There was one death. The authors pointed out that the operation was not without danger and should be used only in severe cases that are not controlled by medication.

Folic Acid Deficiency in Pregnancy.—Megaloblastic anemia is common in pregnancy. It responds to folic acid therapy and is preventable by its administration, suggesting that this form of anemia in pregnancy is due either to a deficient intake of the vitamin or to interference with its utilization. Chanarin and co-workers examined 250 pregnant women to determine whether folic acid deficiency appears in a normal pregnancy and what factors are likely to cause it (*Lancet* 2:634, 1959). The deficiency was measured by the rate of clearance from the plasma of a test dose of injected folic acid. This is cleared from the plasma and passes into the tissues more rapidly than normal in patients with folic acid deficiency. Normal values were first obtained from 50 healthy male and female subjects. Folic acid absorption tests were carried out by giving an oral test dose of 40 mcg. of folic acid per kilogram of body weight and measuring the serum folic acid level. Absorption tests were made by giving 15 mg. of folic acid intramuscularly every day for four days and noting the rate of clearance of the vitamin from the plasma 36 hours later. In normal subjects and those with megaloblastic anemia, folic acid is cleared from the plasma more slowly than in subjects who are not "saturated" in this way.

During the latter part of pregnancy the rate of clearance of folic acid from the plasma was increased in 67% of the women examined and in all women with a twin pregnancy. It was concluded that the increased rate of clearance was due to folic acid deficiency, which the tests showed could have been due to impaired absorption. A deficiency could also have been caused by the folic acid requirement of the fetus exceeding the intake of the mother. The rate of clearance of folic acid from the plasma was even more rapid in 10 women with the megaloblastic anemia of pregnancy. The high incidence of this form of anemia in twin pregnancies, and its onset in late pregnancy, suggested that the factors producing folic acid deficiency in normal pregnancy were responsible for the more severe folic acid deficiency in patients with megaloblastic anemia. Since the absorption of folic acid appeared to be most severely impaired in the pregnant women with megaloblastic anemia, this may contribute to the higher grade of folic acid deficiency found in these patients.

National Health Pensions.—A report by the government actuary revealed a deficiency of 240 million dollars in the pension scheme of the National Health Service between the years 1948 and 1955. This scheme, which is compulsory, covers all employees in the service, including hospital physicians, part-time specialists, general practitioners, and dentists. It was announced in Parliament that a special supplement of 1.5% of salary is to be added to the present contribution by the state to liquidate the deficiency. Employees' contributions will not be raised. The Minister of Health said that about half the deficiency was attributable to the rise in wages and salaries since 1948. If the contributions were to be increased to restore the balance between assets and liabilities, an additional 2% of salary would be required. If the contributions of employees, which in the case of physicians and dentists are disproportionately high, were to be brought in line, an increase in remuneration of 2.5% would be needed, a suggestion that the Ministry of Health has rejected. Instead 95 million dollars will be credited by the government to the pension fund and a supplementary 1.5% of salary will come from the Ministry of Health's salary and wages account. This brings the Ministry of Health's pension contributions to 7.5% of wages for manual workers and 9.5% for other groups, including physicians and dentists. The two latter pay 6% of their salary for pensions.

MEDICOLEGAL ABSTRACTS

Liabilities of Hospital, Surgeon, and Anesthetist for Loss of Teeth During Surgery.—This was an action for damages against a surgeon, an anesthetist, and a hospital for injuries sustained prior to, or during, surgery. Judgments were rendered for the defendants, and the plaintiff appealed to the Supreme Court of Florida.

While inserting a tube into the plaintiff's windpipe in order to supply the lungs with oxygen, the anesthetist, according to her own deposition, heard a faint noise like the cracking of glass. She removed the laryngoscope and examined, visually and with her hand, the patient's mouth. The facing of a tooth came loose and fell in her hand, a peg for a tooth was revealed, and a vacant space next to the peg was discovered. At the conclusion of the operation the anesthetist told the surgeon that one of the patient's teeth had disappeared while the anesthetic was being administered. The anesthetist then searched through the gauze in the waste pail for the missing tooth, but without success. The next day the patient informed the anesthestist that the bridgework consisted of two teeth, and the anesthetist informed the surgeon. Shortly thereafter the plaintiff developed an unproductive cough, and this was noted by the surgeon in the hospital records, but no x-rays were taken in an attempt to locate the missing teeth. Several weeks after the operation, the cough still persisting, the anesthetist suggested that the teeth might be lodged in the patient's lungs. X-rays were then taken and the teeth located in the bronchus and removed.

The Supreme Court said that it was clear that the plaintiff had been attended by a competent surgeon and anesthetist, both of whom knew of the occurrence the very day of the operation. There was no occasion, therefore, to disturb the ruling that the hospital was entitled to a verdict of not guilty. Furthermore, the operation was conceded to have been a success, and nothing appeared in the record suggesting a criticism of the surgeon's exercise of his skill. It was not disputed that the patient's teeth were dislodged while the oxygen was being administered, however, so the principal question was as to the liability of the anesthetist.

From the circumstances leading up to the operation, the Supreme Court determined that the anesthetist could not be said to have deviated from approved practice from the time she began her duties until the operation had been completed. The fact remained, however, that the teeth were broken and lost despite the anesthetist's consciousness of such a contingency. The anesthetist urged that the judgment in her favor should be affirmed, because there was no expert testimony to the effect that she did not perform her function with the same degree of skill and care as any other anesthetist would have used in this operation. However, the court did not think that the plaintiff should be defeated simply because no expert testified that what happened in this case amounted to negligence on the part of the anesthetist. The jury could have decided from common knowledge and experience, regardless of expert testimony, that the patient needlessly suffered from a condition the anesthetist herself sought to prevent. The Supreme Court therefore held that the plaintiff was entitled to have a jury decide whether or not the anesthetist was chargeable with negligence. The court also found no basis for holding the surgeon blameworthy for what occurred while the anesthetic was being given to the patient. The surgeon may have been generally in command from the beginning of the operation to the end, said the Supreme Court, but it is clear that he and the anesthetist were working in highly expert fields peculiar to each and that despite the common goal, the successful repair of the patient's ulcer, their responsibilities were not inextricably bound together.

Accordingly, the judgments in favor of the hospital and surgeon were affirmed and the judgment in favor of the anesthetist was reversed. *Dohr. v. Smith*, 104 So. (2d) 29 (Fla., 1958).

Hospitals in General: Right to Exclude Practitioner.—The plaintiff physician sought to enjoin the defendants from interfering with his right to have private patients admitted into the defendant hospital and to treat his private patients there. From a judgment for the defendants in the trial court, the plaintiff appealed to the Supreme Court of New Jersey.

On Nov. 22, 1952, the plaintiff, then 64 years of age, tendered his resignation from the defendant hospital's active staff, stating that the imminence of the emeritus status (at age 65) made it unwise to reorganize his surgical service for the short time remaining and that he would accept the emeritus rank. He was accordingly elected to the emeritus staff. No duties would thus be assigned to him except in a national emergency, but as a member of the emeritus staff he would be entitled in his private practice to the privileges of the active staff on which he had served for more than 30 years. He remained a member of the emeritus staff until Feb. 16, 1954, when he was advised by letter that he had not been reappointed.

The bylaws of the staff of the defendant provide that, "Before a man fails of reappointment, he shall be given an opportunity to be heard by the Board of Governors if he so desires." A hearing on notice, therefore, is of the essence, and this requirement is not confined to removal or expulsion of an active staff member. The members of the emeritus staff are subject to the same provision. Thus, the action taken by the board of governors was void for want of a hearing in accordance with the defendant's basic law.

The Supreme Court accordingly held that the removal of the plaintiff from the emeritus staff was improper, and the judgment of the trial court was reversed. *Joseph v. Passaic Hospital Association; Joseph v. Barbour*, 141 A. (2d) 18 (N. J., 1958).

Statute of Limitations: Concealment of Right of Action.—This was an action for damages for the alleged unauthorized removal of the plaintiff's gallbladder. From a judgment dismissing the complaint, the plaintiff appealed to the Supreme Court of Wisconsin.

The question for decision was whether or not the action was barred by the statute of limitations. The operation was performed in 1950 and the action commenced in 1956. A cause of action for either assault or malpractice is barred by a two-year statute of limitations. In order to escape the two-year statutes of limitations, however, the plaintiff characterized her action as based on fraud and deceit and claimed the benefit of the six-year statute of limitations.

The court said that the plaintiff alleged no facts which, if proved, would make a case of fraud or deceit. The plaintiff's statement that the defendants had said they would remove only an ovarian cyst and the appendix was not itself a representation of existing fact but rather a statement of intention. There was no allegation that the defendants then intended to remove the gallbladder and that such statement was false or made with intent to conceal a different purpose. No intention to remove the gallbladder was shown or alleged to have arisen prior to the operation, and hence there was no misrepresentation of fact. The plaintiff was notified promptly after the operation that her gallbladder had been removed. There was no false statement of fact and no concealment. Nothing was done by the defendants outside of their professional treatment of her.

When the plaintiff entered the hospital she signed a paper purporting to authorize the physicians in charge to "perform such operations as may be deemed necessary or advisable in the diagnosis and treatment of the patient." The plaintiff alleged that she signed this document without reading it or suspecting its import and that after the operation one of the defendants deceived and misled her by telling her that, by virtue of the consent, he could perform any surgery he chose upon her and there was nothing she could legally do about it. Since the doctor was not alleged to have been a lawyer or to have any greater knowledge of law than the plaintiff, the court stated that his statement cannot be held to constitute actionable fraud.

Accordingly, the Supreme Court concluded, since it appears from undisputed facts shown by the pleadings and affidavits that the cause of action is barred by the statute of limitations, summary judgment was properly rendered for the defendants and such judgment was affirmed. *Suskey v. Davidoff*, 87 N. W. 2d 306 (Wis., 1958).

Privileged Communications in Criminal Cases.—The defendant, being charged with manslaughter, filed a motion for pretrial inspection of certain hospital records and the medical examiner's autopsy report. The motion was heard in the county court, Kings County, New York.

The defendant contended that the blows which he struck were not the cause of the victim's death, but that the victim died of natural causes in a hospital after his admission thereto after the alleged assault. The defendant then insisted that he must be given access to certain records for proper preparation and presentation of his case; namely, the hospital records concerning treatment of the deceased before his death and certain portions of the medical examiner's report with respect to his findings and conclusions as to the cause of death. The district attorney raised the question of the privileged nature of the hospital records and contended that the autopsy report was not available because of a state statute.

The court said that, generally speaking, physical objects, documents, hospital reports, chemical analyses, blood tests and related reports may be made available to a defendant before trial in the discretion of the court. It need not appear that such evidence is relevant, competent, and outside any exclusionary rule. The court also said that, because of the privileged communications statute, a hospital record will nevertheless be excluded if it discloses any information which the physician acquired in attending a patient in a professional capacity and which was necessary to enable him to act in that capacity. In civil cases, therefore, if the patient is a party to the proceedings, the defendant cannot invoke the privilege; only the patient may invoke or waive the privilege. The privilege cannot be claimed by a party where the patient is not a party to the proceeding.

In criminal cases, where the defendant is the patient, he may claim the privilege or waive it. Under no circumstances, however, may a defendant invoke his victim's privilege. The purpose of the physician-patient privilege is to protect the patient, never to shield the criminal.

The main issue in the instant case, said the court, is whether or not the People may under any circumstances invoke the privilege. In the opinion of the court, the same reasons which deny to the defendant the right to invoke his victim's privilege also prevent the People from invoking the privilege of the complaining witness. The privilege belongs to the patient and the patient alone may claim it. Under no circumstances may the People invoke the physician-patient privilege. Furthermore, the People may not in any criminal case withhold evidence which could conceivably disprove or tend to disprove the defendant's guilt. If, in the instant case, the hospital record would tend to disprove the defendant's criminal agency in causing the death of the deceased, such evidence may not be withheld by the People on any claim of privilege or under any other rule of evidence. Such withholding may violate due process under both the state and federal constitutions.

With respect to the portions of the medical examiner's report sought to be inspected, the pertinent provision of the New York City charter provides that "such records shall not be open to public inspection." This provision, said the court, was not intended to preclude a defendant from inspecting the medical examiner's report of his autopsy. In all counties outside New York City such autopsy reports are specifically made available to the defendant by order of a court. The legislature did not intend to establish one rule for New York City and another for the rest of the state. It intended that a medical examiner's report indicating criminality shall be kept secret from the general public. The charter provision is another safeguard devised by the legislature to protect the rights of the accused. Autopsy reports where no evidence of criminality is indicated, however, while not available to the public, are available to any defendant by order of a court.

Accordingly, the court ruled that the defendant may, in the discretion of the court, be granted the right to inspect certain portions of the medical examiner's report relating to the autopsy and the hospital record. *People v. Preston*, 176 N. Y. S. (2d) 542 (N. Y., 1958).

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The defendant received a letter from a doctor in another state requesting information about the plaintiff, a former patient of defendant. The letter asked for "your impression of the man," for the purpose of passing it on to the parents of a girl who was then keeping company with the plaintiff. The defendant wrote that, seven years before, the plaintiff had been having marital difficulties and, at the request of his then wife, had gone to the defendant. His condition was diagnosed; electric shock treatments were recommended and four were given. The defendant added that he had not seen the plaintiff since that time. This letter was relayed by the Wyoming doctor to the girl's parents and in turn to their daughter. The parents became violently opposed to the marriage and have since disowned the girl because she and the plaintiff are now husband and wife.

Ordinarily, said the Supreme Court, the truth is a defense to an action for libel or slander. In the instant case, however, there is a special circumstance to reckon with, i. e., a doctor-patient relationship existed between the parties, and the information contained in the letter arose out of such a relationship. It is the policy of the law to encourage confidence in this relationship. If a doctor could with impunity publish anything, so long as it is true, the patient would be without protection from disclosure of intimacies which might be both embarrassing and harmful. This might make the patient reluctant to tell some things even though they might be important in his treatment. Therefore, it is the doctor's obligation not to reveal information obtained in confidence in connection with the diagnosis or treatment of his patient. If the doctor violates that confidence and publishes derogatory matter concerning his patient, an action would lie for any injury suffered.

The defendant contended that the responsibility of a doctor to keep confidence may be outweighed by a higher duty to give out information, even though defamatory, if there is a sufficiently important interest to protect. In such an event there arises a conditional privilege to make a disclosure reasonably necessary to protect such interest.

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MISCELLANY

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Modern research has thrown new light upon the age-old dispute over the relative importance of inheritance versus environment, of instinct versus learning. Every living organism, including man, has a genetic constitution which establishes and limits the potential for growth, differentiation and life span. Every manifestation of structure, function or behavior is determined by the interaction of the organism with its environment and becomes an essential element in each phase of growth, development and aging. These dramatic developments along with the new understanding of mutations which may be brought about by radiation have awakened great interest in medical genetics, a discipline which will have a profound impact upon the whole field of reproduction, congenital anomalies, chemical as well as anatomical, and a wide range of clinical manifestations.

The discovery that many diseases may be due to the genetically determined absence or reduction in amount of a single enzyme adds great importance to some new concepts of growth, physiology, infection and disease. The advances in biochemistry, in tissue culture, in electrophoresis and paper chromatography, combined with a knowledge of the principles of genetics, offer special opportunities not only for diagnosis and prevention but also for treatment. The metabolic disorders (diabetes, nephritis), the degenerative diseases (cirrhosis, arthritis, certain mental disturbances, arteriosclerosis), some malignant conditions, nutritional inadequacies and other major handicaps may well involve a genetic factor. Many diseases are in reality combinations of constitutional and environmental factors. Sometimes too much emphasis has been placed on the trigger mechanism of the environment and too little on the factors of inheritance and susceptibility. An understanding of certain disturbances in the human being is now possible through the application of recently acquired knowledge of enzymatic and biochemical processes.

The recent contributions of organic chemistry to studies in arteriosclerosis are widely known. The whole field of nutrition is based on an understanding of underlying biological chemistry. Kidney, liver, heart, brain and endocrine functions can only be understood in the light of physiological interplay. The nerve impulse itself is now recognized as a chemical or electrochemical process elucidated by years of laboratory research in advanced physics and chemistry. Studies on viruses and bacteria by intensive techniques and new instruments promise to throw light on the origin of life itself. What additional knowledge will come from or be needed for space medicine is still unknown. The many contributions of the sciences have introduced a wide range of quantitative methods into medical teaching, research and practice, sometimes obscuring the human and emotional factors in illnesses which as yet do not lend themselves readily to quantitative measurements.

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prove the defendant's guilt. If in the instant case, the hospital record would tend to disprove the defendant's criminal agency in causing the death of the deceased, such evidence may not be withheld by the People on any claim of privilege or under any other rule of evidence. Such withholding may violate due process under both the state and federal constitutions.

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The court agreed with this contention and stated further that such a privilege may extend to the protection of the interests of third persons under proper circumstances, as where life, safety, well-being or other important interest is in jeopardy. The trial court found that the circumstances here came within the framework of conditional privilege: that is, that the girl's concern for her well-being and happiness was a sufficient interest to protect and that it was within the generally accepted standards of decent conduct for the doctor to reveal the information which might have an important bearing thereon. That is as far as the trial court could go, however, said the Supreme Court. In submitting the case to the jury on the basis of privilege, therefore, it was necessary to instruct as to the limitations on the manner in which the privilege should be exercised. The conditional privilege, the Supreme Court held, must be exercised with these certain cautions: 1. It must be done in good faith, and reasonable care must be exercised as to the truth. 2. The information must be reported fairly. 3. Only such information should be conveyed and only to such persons as are necessary to the purpose. The evidence provided a basis on which reasonable minds might differ as to whether the defendant did that which was discreet and proper with respect to these principles in connection with the passing on of information of the character in question. Such issues should have been submitted to the jury. Inasmuch as the manner in which the case was submitted did not permit the jury to pass on these issues, the Supreme Court remanded the cause for a new trial. Judgment for the defendant physician was reversed. *Berry v. Moench*, 331 P. 2d 814 (Utah, 1958).

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Anatomicoelectrocardiographic Study of 15 Lateral Myocardial Infarctions. J. Himbert, J. Lenègre and S. Tintoret-Ferrer. Arch. mal. coeur 52:841-860 (Aug.) 1959 (In French) [Paris].

Records of 15 cases of pure lateral infarction, which represented 7.3% of the autopsy records of myocardial infarction at the Boucicaut Hospital in Paris for the period 1949-1956, were studied in an attempt to compare the electrocardiographic findings with the anatomic lesions found at autopsy. This series comprised the records of 12 men and 3 women, between the ages of 46 and 77 years. The etiological factor was traced to cardiopathy caused by coronary atherosclerosis. In 5 cases there had been simple coronary atherosclerosis; in 8 the atherosclerosis had been associated with arterial hypertension, in 1 with syphilitic aortitis, and in 1 with aortic stenosis. In 8 patients the infarction had affected less than 25% of the endocardial surface of the left ventricle; in 7 it had affected more than 25% and less than 50% of this surface. In 13 patients the area involved represented from 10 to 30% of the left ventricle; in one this area had been particularly small, occupying less than 10% of the left ventricle; and in another it had been rather large and had destroyed almost half of the left ventricular muscle.

In 9 electrocardiograms there were traces of necrosis (significant initial Q wave or abnormal Q-S wave) associated or not with lesion or subepicardial ischemia. Indirect signs of lateral necrosis were found in one electrocardiogram in the form of initial and predominant positivity, with the R/S ratio larger than in leads VE, V_1, V_2, and V_3. Direct signs of subendocardial lesions were found in one record, and indirect signs in another. Direct signs of ischemic lesion or of subepicardial ischemia were observed in the 9 electrocardiograms which contained signs of necrosis and in 4 of the 6 without these signs. Indirect indications of lateral subepicardial ischemic lesion were also observed in 2 electrocardiograms in the form of inferior deviation of the S-T segment, coupled with a relatively wide and sharp positive T wave visible in leads V_1, V_2, and V_3.

The following correlations were found: Ten electrocardiograms suggested myocardial infarction—in 9 cases because of a necrotic wave, and in one because of a major and durable subendocardial ischemic lesion. Three electrocardiograms raised suspicion of myocardial infarction—one by signs of a well-defined subendocardial ischemic lesion, and 2 by signs of posterolateral subepicardial ischemic lesion. Two electrocardiograms were nonrevealing and showed only indications of lateral subepicardial ischemia associated with nondecisive signs of a discrete subepicardial lesion. The diagnosis of infarction had been established by electrocardiography in 5 of 8 patients who had had recent attacks and in 5 who had had old infarction (longer than 6 weeks before death). Transmural infarctions were recognized in 6 cases and were suspected in 2. Nontransmural infarctions were often recognized (4 cases) or suspected (1 case) but sometimes missed (2 cases). Even when recognized or suspected, as happened in 13 cases of this series, the infarction was not always exactly located. It was erroneously considered as posteroinferior in one case and posterolateral in 4 cases.

The study indicates that pure lateral infarctions are rare. Their identification is obtained in only approximately two-thirds of the cases because of the reduced extent of muscular destruction and of the multiple possibilities of orientation in the lateral ventricular wall. It seems advisable, when the usual leads are silent or undecisive, to register supplementary leads (V_8, V_9, high precordial series), to take into consideration the indirect signs registered in the precordium on the right, to interpret as danger warning minor but persistent signs registered in the lateral leads, and to compare in detail the suspect electrocardiogram with previous ones if they are available.

The Use of L-Lysine Monohydrochloride in the Treatment of Mercurial-Resistant Edema. D. Brailovsky, C. Silva, E. Del Campo and E. Marusic. Am. J. M. Sc. 238:287-296 (Sept.) 1959 [Philadelphia].

L-lysine monohydrochloride was administered in daily doses of 10 to 40 Gm., for periods of 5 to 47 days, to 45 ward patients to restore responsiveness

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The place of publication of the periodical appears in brackets preceding each abstract.

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to mercurial diuretics. Five patients were eliminated because of immediate gastrointestinal manifestations. In the remaining group Laennec's cirrhosis was present in 13 patients, heart disease in 24, bronchial asthma, chronic nephritis, and rheumatoid arthritis in 3. There was a mercurial-resistant group of 18 patients, and a trial group of 22. The reason for the trial group was to study the chloride liberating capacity of the drug and the tolerance of the product.

The administration of L-lysine monohydrochloride did not produce any changes in plasma and urinary sodium and potassium levels. The drug produced statistically significant increase in plasma and urinary chloride levels in both the mercurial-resistant group and the trial group, except in 2 patients of each group. It also produced statistically significant fall of plasma carbon dioxide combining power, except in 5 patients. In the 18 mercurial-resistant patients, the combination of L-lysine monohydrochloride and mercurial failed in only 2; both these patients were in far-advanced stages of fluid retention. The drug, on a whole, was well tolerated, although 2 patients had nausea, 4 had nausea and vomiting, and 1 had nausea, vomiting, and diarrhea. Precoma states developed in 2 patients with Laennec's cirrhosis, one of whom died of hemorrhage from ruptured esophageal varices. The results of this study point out that L-lysine monohydrochloride is a good source of chloride in the treatment of patients with mercurial-resistant edema.

The Arthritis of Ulcerative Colitis. V. Wright and G. Watkinson. Medicine 38:243-262 (Sept.) 1959 [Baltimore].

The authors report on 42 male and 66 female patients, between the ages of 14 and 79 years, who were treated for ulcerative colitis at the General Infirmary or St. James's Hospital in Leeds, England, between 1955 and 1958. Combined assessment by a gastroenterologist and a rheumatologist made it possible to correlate arthritic symptoms with those of colitis. In 17 (15.7%) of the 108 patients, arthritis developed, which seemed to be of a specific type and to be related to the associated colitis. This type of arthritis was designated as "colitic arthritis." It occurred in 5 men and 12 women; the onset of arthritic symptoms was acute in 9 patients and insidious in the remaining patients; it affected one joint only in 9 patients and several joints in the other patients. Thirty-two attacks of colitic arthritis occurred in the 17 patients, and the joints most commonly involved in the first and in the recurrent attacks were the knees and ankles. It appeared that colitic arthritis is characterized by a recurrent acute synovitis, usually monarticular and asymmetrical, attacks being of short duration and unaccompanied by residual deformity or radiologic change. Exacerbations of arthritis were usually associated with increased intestinal symptoms and accompanied by constitutional disturbances.

The combined assessment revealed that the colitic arthritis occurred more commonly in patients with chronic colitis of prolonged duration and with more extensive involvement of the colon. It developed more frequently in patients with local or systemic complications, such as skin lesions, recurrent ulcers of the mouth, and uveitis. Colectomy and salicylate and steroid therapy frequently induced remissions, but these usually occurred spontaneously. When the clinical features of 95 unselected patients with uncomplicated rheumatoid arthritis and a positive reaction to the sheep-cell agglutination test were compared clinically and radiologically with those of the 17 patients with colitic arthritis, important differences emerged which made it evident that there were no grounds for regarding colitic arthritis as a variant of rheumatoid arthritis. Its distinction from ankylosing spondylitis appeared to be less well defined.

Clinical and Anatomic Study of 60 Cases of Malignant Hypertension. M. P. de los Reyes, R. Cruz-Coke and U. Urozco. Rev. méd. Chile 87:603-609 (Aug.) 1959 (In Spanish) [Santiago].

The results of medical, surgical, and medicochirurgic treatment of 60 patients hospitalized because of malignant hypertension are reported. There were 31 males and 29 females in this series, between the ages of 10 and 70 years, with the greatest frequency (approximately 70%) in the 5th and 6th decades of life. The degree and malignancy of the hypertension, as well as the renal and cardiac involvement, were evaluated by clinical and laboratory studies. In 22 patients it was possible to perform histopathological examination of the kidneys, either at autopsy or by biopsy during the operation. The hypertension was diagnosed as essential when a thorough examination, especially of the kidneys and the urinary tract, showed no evidence of any disorder which could be responsible for the blood pressure state. Arterial hypertension was essential in 18 patients (30%), and it was secondary to pyelonephritis in 25 (41.6%), to chronic glomerulonephritis in 13 (21.6%), to diabetic nephropathy in 1; it was undetermined in 3 patients. The most frequent diagnoses among the male patients were essential hypertension and hypertension secondary to chronic nephritis; for the females the diagnoses were hypertension secondary to chronic pyelonephritis and essential hypertension.

All the patients were treated with bed rest, a strict low-salt diet, and a combination of hypotensive drugs. Most of them received reserpine (0.75 to 1.0 Gm. daily) and pentolinium (120 to 300 mg. daily). Some received hydralazine (150 to 200 mg. daily). Surgical treatment was given to 10 patients and consisted of dorsolumbar sympathectomy (performed on 5 patients), unilateral nephrectomy (on 4), and correction of urinary abnormalities (on 2). Immediate results of the medical therapy are given for 38 patients; they were good (diastolic pressure decreased to 105 mm. Hg or less) in 26 patients (68.4%) and fair (arterial pressure of 110-115 mm. Hg or less) in 4 patients (10.5%). Since an arterial pressure of 120 mm. Hg or higher persisted in 8 patients (approximately 21%), they were considered failures. Late results (within 1 to 6 years) are reported for 14 patients who could be followed up. According to the criteria used to evaluate the immediate results, they were good in 6 patients, fair in 2, and negative in 6. The results of the surgical treatment were discouraging. The 5 sympathectomies and the 2 corrective operations of the urinary tract were complete failures. Of the 4 patients treated with nephrectomy for chronic pyelonephritis, only one obtained permanent good results.

In this series of 60 patients, 35 were followed up, and 21 of these 35 died. This mortality rate, however, cannot be considered as valid for the whole group, since 25 patients (40%) were not included in the final evaluation.

Persistence of Antibiotics in Blood of Patients with Acute Renal Failure: I. Tetracycline and Chlortetracycline. C. M. Kunin, S. B. Rees, J. P. Merrill and M. Finland. J. Clin. Invest. 38:1487-1497 (Sept.) 1959 [New Haven, Conn.].

Severe renal disease is frequently complicated by infections. Overwhelming infection, particularly with gram-negative bacteria, is often associated with shock and anuria, and antibiotic therapy is an integral part of the management in such cases. Knowledge concerning the fate of antibiotics in patients with impaired renal function is, therefore, necessary for planning therapy, so that it will insure adequate blood and tissue levels without undue retention that may be harmful. A series of studies was undertaken in patients with anuria or impaired renal function from various causes, who either were receiving antibiotics as part of their therapy or were given test doses of some of the commonly used antibiotics.

It was found that the half-life of intravenously administered tetracycline in persons with normal renal function was about 6 or 7 hours when measured by the twofold dilution method. With decreasing renal functional capacity as measured by the endogenous creatinine clearance, the half-life was prolonged and markedly so when the creatinine clearance fell below 30 ml. per minute; in the anuric patients it was as long as 4 or 5 days. Tetracycline is cleared to a less extent than is creatinine or urea by hemodialysis across the artificial kidney; this is presumed to be due to the binding of the antibiotic to the plasma proteins.

In contrast to the findings with tetracycline, the half-life of chlortetracycline in the serum of patients with severe renal disease was only slightly elevated above normal values, and hemodialysis by the artificial kidney did not result in lowering of the serum levels of this drug. The reasons for concluding that this difference is due to the rapid in vivo inactivation of this antibiotic are discussed. The poor extraction of tetracycline, and particularly of chlortetracycline, by the artificial kidney is interpreted as being the result of the binding of these drugs to serum protein. The implications of these data for the potential toxicity of these drugs in uremic patients are discussed, and an empirical dosage schedule is offered for use in such patients.

A Further Contribution to the Problem of the Diagnosis and the Pathogenesis of Edematous Pictures After Anicteric Acute Hepatopathy. F. Di Lollo. Sett. med. 47:373-379 (Aug. 15) 1959 (In Italian) [Florence, Italy].

The cases of 3 patients who presented secondary edema during the course of anicteric acute hepatitis are reported. The first patient, a 25-year-old man, several years before presenting edema had been subjected to gastric resection for duodenal ulcer; on observation, he presented edema in the lower limbs and in the face, anemia, lambliasis, oliguria, dyspeptic disturbances, lack of appetite, and marked asthenia. The transudation lasted for about 2 months and disappeared after the occurrence of a marked diuresis. There is doubt whether transudation was caused by the hepatopathy or by the gastrectomy which at times generates edema because of the malnutritional hypoproteinemia resulting from it. The patient was treated for a month with liver extracts, vitamin C, vitamin-B complex, and amino acid solutions; he received 4 plasma transfusions during the first 10 days of hospitalization; the lambliasis was treated with Atabrine. The second patient, a 57-year-old man, had suffered from chronic endocarditis; the edema, however, appeared independently of the cardiopathy, at the end of an episode of fever which lasted for several days and was accompanied by oliguria and hepatomegaly of rather recent date. Edema lasted for about a month and disappeared after marked diuresis. The patient was treated with liver extracts and vitamins B and C. The third patient, a 24-year-old man, had suffered for some time from colitis. The transudation, which appeared after a period of fever and intestinal disturbances, resulted in a true anasarca which lasted 25 days and disappeared after the occurrence of a marked diuresis. Forty days after recovery the patient suffered from polyradiculitis of the Guillain-Barré syndrome type. Three years later he died of a hemorrhage due to rupture of an esophageal varix.

The author believes that edema in the course of acute hepatopathy is due to the anicteric variety of acute viral hepatitis, which may also develop into a cirrhosis; that the disease of the liver may affect in degree, intensity, and length of time the various functions of the liver; and that the diagnosis in such cases depends on the absence of the usual causes of edema and on the presence of clinical and biochemical signs of liver involvement. He also believes that the pathogenetic mechanism of the transudation is caused by a plasmatic "hyponchia" (osmotic hypotonicity of the plasma) caused by a decline in albuminemia and an increase in the tubular readsorption of water and sodium chloride.

D-Xylose and Its Use in the Diagnosis of Malabsorptive States. P. A. Christiansen, J. B. Kirsner and J. Ablaza. Am. J. Med. 27:443-453 (Sept.) 1959 [New York].

The studies described were undertaken to evaluate the oral D-xylose test and to compare it with other indexes of absorption in patients with malabsorptive states of varying etiology. Xylose is a 5-carbon monosaccharide (pentose) with a molecular weight of 150. Foodstuffs, such as fruits and grains, are especially rich in pentoses and can produce an alimentary pentosuria. As with most simple carbohydrates given alone or after digestion of a balanced meal, xylose is absorbed (translocated) primarily in the duodenum and the proximal jejunum. The normal metabolic fate of D-xylose in the body is described as a background for evaluating the use of xylose as a test of intestinal absorption. The test is performed by measuring the excretion of D-xylose in the urine after the oral administration of 25 Gm. The results of the xylose test in more than 100 patients have been compared with other measurements of intestinal absorption in the same patients, and indicate the wide applicability and the relative simplicity of the procedure.

Less than 2.5 Gm. of xylose (10%) is excreted in a 5-hour urine collection in patients with untreated idiopathic malabsorption; xylose excretion usually remains low despite treatment. Other tests in untreated patients with idiopathic malabsorption also demonstrate defective absorption of carotene, fat, and glucose. In patients with pancreatic disease the xylose test is normal, although other absorptive tests, e. g., fat absorption, may be abnormal. The results of fat absorption, carotene, and xylose tests do not correlate consitently in any condition other than idiopathic malabsorption. Except in patients with idiopathic malabsorption, few subjects excrete less than 2.5 Gm. of xylose. The D-xylose test appears to be the most useful screening procedure for identifying idiopathic and secondary types of malabsorption or steatorrhea currently available.

Hodgkin's Disease Associated with Other Malignant Tumors and Certain Non-neoplastic Diseases. D. V. Razis, H. D. Diamond and L. F. Craver. Am. J. M. Sc. 238:327-335 (Sept.) 1959 [Philadelphia].

The authors investigated the incidence of secondary primary tumors and certain nonneoplastic diseases in 1,102 patients with Hodgkin's disease, in 1,269 patients with lymphosarcoma, and in 220 patients with leukemia. A second primary tumor was found in 24 patients (2.2%) of the Hodgkin's disease group, in 48 patients (3.9%) of the lymphosarcoma group, and in 5 patients (2.3%) of the leukemia group. Chronic lymphocytic leukemia was the type most often associated with carcinoma, especially that of the skin. In the lymphosarcoma group, 3 of the 48 patients with a second primary neoplasm also had a third primary tumor. Kaposi's sarcoma coexisted in 2 patients with Hodgkin's disease. Two patients had Hodgkin's disease associated with reticulum-cell sarcoma. Leukemia developed in 2 patients (0.18%) with Hodgkin's disease.

Active tuberculosis was associated more often with Hodgkin's disease (20 patients) than with lymphosarcoma (4 patients). Collagen disease was present in 3, possibly 4 patients with Hodgkin's disease but in none of those with either lymphosarcoma or leukemia. Two patients gave a history of idiopathic thrombocytopenic purpura, beginning 12 and 15 years before the onset of Hodgkin's disease. Both patients were successfully treated by splenectomy. Diabetes mellitus was found in 26 of the 1,102 patients (2.36%) with Hodgkin's disease, in 37 patients in the lymphosarcoma group (2.9%), and in 1 patient in the leukemia group. Secondary amyloidosis was found in 5 patients out of the 234 examined at autopsy, but in no patient with lymphosarcoma and leukemia. It seems that nitrogen mustard was not a causative factor of the secondary amyloidosis. There was association of syphilis with Hodgkin's disease in 11 patients and with lymphosarcoma in 1.

Salt-Wasting Renal Disease: Metabolic Observations on a Patient with "Salt-Losing Nephritis." S. W. Stanbury and R. F. Mahler. Quart. J. Med. 28:425-447 (July) 1959 [London].

Since the syndrome of "salt-losing nephritis" was first defined by Thorn, Koepf, and Clinton in 1944, observations on about a dozen patients have been described, and fragmentary metabolic studies were made on some of them. This report is concerned with comprehensive metabolic studies on a woman, who was 32 years old in 1954, and who gave no history of past renal disease or of renal symptoms. For several years she had been accustomed to drink copious amounts of fluid and admitted to taking up to 15 cups (about 7 oz., or 200 ml., in capacity) of tea in the course of a day. In February, 1954, the patient's wisdom teeth were extracted under local anththesia. She vomited frequently during the following day, and thereafter progressive lassitude developed. On getting up after a few days' rest in bed, she experienced severe postural giddiness. These symptoms and a troublesome nausea improved within a month, but she remained in poor health, and lost abaut 10 lb. (4.5 kg.) in weight. She was easily tired and dyspneic on exertion; a rapid change of posture would produce giddiness and sometimes a transient impairment of vision.

When vomiting commenced again in May, 1954, the patient was hospitalized. Examination revealed moderate anemia, a faintly bronzed facial skin, and dark nipples and areolas. The arterial blood pressure fell on standing. The sodium content of the serum was diminished, and the potassium content was increased. The blood urea level was 115 mg. per 100 ml., the hemoglobin value was 9 Gm. per 100 ml., and the erythrocyte count was 3,230,000 per cubic millimeter. The electrocardiogram showed the peaked T waves of hyperkalemia. n the absence of renal symptoms and proteinuria, a diagnosis of Addison's disease was made, and appropriate therapy instituted, after which the patient's clinical condition improved rapidly. Later it was realized that the patient had a "salt-wasting' renal lesion, and further metabolic investigations were carried out.

In the summary, the authors say that, in spite of a grossly impaired renal capacity to conserve sodium, the loss of sodium in this patient was limited by a progressive fall in its urinary output toward the level of dietary intake. The acutely developing deficiency of sodium initiated a catabolic response that contributed to the production of increased serum levels of urea and potassium. The renal capacity to vary the output of potassium was limited, and the serum level of potassium was determined primarily by shifts of this ion between cells and extracellular fluid with changes of acid-base balance. The urinary output of aldosterone was greatly increased long after the deficiency of sodium had been corrected. It is suggested that the adrenal secretion of aldosterone may become autonomous after a prolonged period of stimulation. Attention is drawn to the gross adrencortical hyperplasia in the recorded autopsies in "salt-losing nephritis."

It is suggested that the pattern of renal function in azotemic renal failure is compatible with a constantly operating osmotic diuresis, which results from the entry of an increased load of solute into the surviving nephrons. Reduced tubular reabsorption of sodium and chloride would follow as a physiological consequence of osmotic diuresis; and, in the "salt-wasting" syndrome, the greater renal loss of salt may result simply from a quantitatively greater osmotic loading and a consequently more intense osmotic diuresis. After the therapeutic provision of a supplement of sodium salts, a greater load of sodium is filtered into each nephron; the osmotic effect of this additional sodium increases the tubular diuresis and reduces the reabsorption of urea and water. The result is an increase in urinary volume and a fall in the body content of urea.

SURGERY

A Study of Fatal Breast Cancer. R. W. Powell and D. R. Rooney. Am. Surgeon 25:692-697 (Sept.) 1959 [Baltimore].

The authors report on 239 women who died of breast cancer. The patients received their initial treatment at the Robert Winship Memorial Clinic and in the department of radiology, Emory University Clinic, Atlanta, Ga., between 1937 and 1957. Of the 239 patients, 170 were subjected to a radical mastectomy, and those in whom positive axillary lymph nodes were proved microscopically were given postoperative roentgenotherapy. The remaining 69 patients had inoperable tumors and were treated in the same manner as those with operable tumors who had recurrence of the disease, that is, with roentgenotherapy, hormones, extirpation procedures, chemotherapy, supportive care, and a combination of these treatments. The mean age of the patients in the first group was 51.8 years; of those in the second group it was 57 years.

Three findings of special interest were obtained in this study: 1. Longevity in these patients, computed from the appearance of the initial symptom or from the time of original therapy to death, is not greatly altered by any present treatment. 2. Once breast cancer becomes clinically manifest as a recurrence or as metastases, longevity, computed from the date of recurrence to death, is not greatly affected by either the original stage of the disease or the "disease-free" interval. 3. In 99 of the patients who were operated on, the intial recurrences were first clinically detected as distant metastases. It is in this group that longevity should be increased when methods become available to prevent or to treat blood-borne metastases.

It is emphasized that no attempt has been made in this study to evaluate the patients' comfort. Since treatment apparently does not prolong life in such patients, their comfort becomes the most important goal of therapy. These findings are not to be construed as a condemnation of present therapeutic methods; instead they should be regarded as a stimulus to further research in the therapy of cancer of the breast.

Reno-Mesentero-Aorto-Iliac Thromboendarterectomy in Patient with Malignant Hyptertension. T. E. Starzl and O. H. Trippel. Surgery 46:556-564 (Sept.) 1959 [St. Louis].

Early attempts at surgical treatment of occlusive arterial disease were focused on the lower extremities, not only because of the prevalence of involvement there, but because the symptoms of arterial insufficiency were clear-cut and methods of diagnosis were precise. In contrast, ischemia of visceral organs often resulted in vague symptoms, and diagnostic methods were frequently inexact. A further deterrent to reconstructive arterial surgery was the widely held view that major vessel occlusion to many visceral tissues would result in irreversible damage with such rapidity that reconstitution of arterial blood flow would be fruitless. It is now realized that this is often not the case and that all tissues of the body (under the appropriate circumstances) may react to extensive devascularization with diminished function rather than by necrosis.

The authors report on a 62-year-old man who presented with malignant hyptertension, intermittent claudication, and abdominal complaints suggestive of "intestinal angina." There was complete occlusion of the left renal artery and partial occlusion of the right renal and superior mesenteric arteries, complicating extensive aortoiliac thrombosis. Treatment consisted of thromboendarterectomy of all involved vessels, after which the patient became normotensive and all abdominal symptoms subsided. The case is thought to be the first successful bilateral simultaneous renal endarterectomy, and the third successful case of superior mesenteric endarterectomy.

Phaeochromocytoma: A Report of Seven Cases. J. De Graeff, H. Muller and A. J. Moolenaar. Acta med. scandinav. 164:419-430 (no. 5) 1959 (In English) [Stockholm].

The authors report on 7 patients with pheochromocytoma. A pheochromocytoma was removed from the right adrenal in one patient; tumor in the hilus of the right kidney was removed on second operation 3 years later; there was no evidence of a relationship between the 2 tumors. A second patient died 24 hours after removal of a pheochromocytoma of the right adrenal. At autopsy a pheochromocytoma of the left adrenal and an anaplastic thyroid carcinoma with pulmonary metastases were found. An extra-adrenal pheochromocytoma was localized in the thorax in 2 more patients. This incidence suggests a more thorough roentgenologic examination of the supradiaphragmatic, paravertebral region in patients who had or are suspected of having a pheochromocytoma. An extra-adrenal pheochromocytoma was found below the right renal artery in a 5th patient. Communication between the extra-adrenal pheochromocytoma and the sympathetic trunk or splanchnic nerve was established in all instances. One patient was admitted to the hospital in a shock-like condition accompanied by vomiting. She complained of previous episodes of dizziness and vague abdominal pain. She died within 36 hours in a state of progressive, irreversible shock with terminal hyperthermia. Massive hemorrhage in a pheochromocytoma of the right adrenal was established on autopsy.

The intravenous injection of 5 mg. of phentolamine, which was used as a screening test for pheochromocytoma, produced a marked decrease in blood pressure in all 5 patients to whom it was administered. A positive test for pheochromocytoma with phentolamine was checked by the benzodioxane test. If both these tests were positive, they were double-checked by measuring the excretion of catechols.

A Study of Pneumothorax Therapy and Its Long-Term Results. I. Alonen and J. N. Mäkipaja. Acta tuberc. scandinav. 37:175-186 (no. 3) 1959 (In English) [Copenhagen].

The use, complications, duration, and long-term results of 401 pneumothoraces induced in 381 patients at the Central Sanatorium of Middle Finland during 1947-1949 are analyzed. There were 211 males and 170 females; their ages ranged from 11 to 55 years, with the greatest frequency in the 21-30 age bracket. At the time of this investigation there were 341 surviving patients, in whom 356 pneumothoraces had been induced; 259 of the pneumothoraces had been preceded by sanatorium treatment for 2 months or less, and 97 by a period of treatment of more than 2 months. At the time of the initial pneumothorax therapy, 88.8% of the patients had positive cultures. The patients with negative sputum findings were also included in the treatment, because their clinical picture was typical of tuberculosis.

Of the patients who received less than a 2-month preparatory treatment, 56.8% originally had no adhesions or were freed by adhesion section, and 43.2% had an incomplete pneumothorax. Among those who received more than a 2-month preparatory treatment, these percentages were, respectively, 57.7 and 42.3%, which seem to indicate that in this series the duration of preparatory treatment did not influence the occurrence of adhesions. Complications occurred in 50.8% of the patients with complete, and in 58.7% of those with incomplete pneumothorax. Pleural effusion or contraction or both formed the largest group of complications and the main reason for premature termination of the treatment. Empyema and atelectasis played only a minor role. The duration of 277 full-term, effective pneumothoraces, which represented 81.6% of the total number, was 2 to 4 years, whereas 79 (22.2%) were terminated because of ineffectiveness, complications, occurrence of spontaneous pneumothorax, or aggravation of the patient's conditions.

Of the 381 patients studied, 320 were treated by pneumothorax alone. At the end of the treatment, 271 (84.7%) were considered to have inactive tuberculosis. Taking into consideration the patients who died (approximately 10% of the original number), the ultimate results were found to be considerably poorer in exudative than in productive tuberculosis. Exudative tuberculosis was inactive in 63.4% of the patients with cavitation, and in 62.8% of those without cavitation. In productive tuberculosis these percentages were, respectively, 83.5 and 71%. As 78.5% of the patients in this series were capable of work at the time of this investigation, the results of the pneumothorax therapy were considered good. It is the authors' opinion that pneumothorax can well be retained among the therapeutic methods for pulmonary tuberculosis, for it is a reversible procedure, and complications can be fairly readily managed with modern medical therapy.

Blood Transfusions and Serum Hepatitis: Use of Monochloroacetate as an Antibacterial Agent in Plasma. J. G. Allen, D. Dawson, W. A. Sayman and others. Ann. Surg. 150:455-468 (Sept.) 1959 [Philadelphia].

The data reviewed were obtained from a survey of patients receiving blood transfusions without plasma at the University of Chicago Clinics during the years from 1946 to 1956. Random sampling of a total of 11,382 patients resulted in the selection of approximately 21% of the total group, that is of 2,388 patients, who received blood only (no plasma). An "average" of 3 units of blood was given each of the 2,388 patients in the series. Serum hepatitis developed in 36 and jaundice (in which the diagnosis of hepatitis was doubtful) in 8 of the 2,388 patients, of whom 1,892 survived at least 6 months after their last blood transfusion. Five of the 36 patients and 2 of the 8 patients in whom the diagnosis was questionable died. Donor sources were of 2 types: (1) family donors (relatives and friends of the patient) and (2) professional donors. The incidence of serum hepatitis was from 7 to 10 times as high after transfusions of blood from professional donors as after transfusions from family donors. With single unit transfusions, the attack rate was 0.3% with family donors and 3.2% with professional donors.

The risks of and the measures taken to avoid bacterial contamination of bank blood are discussed. Data are presented on the antibacterial (bactericidal) activity of the sodium salt of monochloroacetic acid when added as 1-molar solution to citrated blood or plasma, so that its final concentration was 0.02 M or 0.04 M per liter of plasma or blood. This agent proved successful in eradicating heavy bacterial contamination with human pathogens. Plasma to which the acetate had been added displayed little, if any, detectable change in its electrophoretic pattern, viscosity, or optical density.

Acetate-treated plasma was transfused to dogs in daily volumes equal to 50% of the animal's estimated plasma volume for periods of 28 to 42 days. No abnormal physiological reactions or pathological effects were observed. The animal's response to transfusions of acetate-treated plasma was not different from that of ordinary citrated plasma. To date, 11 debilitated patients with advanced carcinomatosis have received a total of 53 units (550 ml. each) of pooled plasma containing 0.02 M or 0.04 M of acetate. The conditions of all were improved clinically to the extent expected from the administration of similar volumes of ordinary plasma.

Citrated whole blood to which monochloroacetate had been added (human and canine) gave no evidence that the life span of red blood cells was shortened, that the oxygen-carrying capacity of erythrocytes was altered, that red blood cell fragility was increased, or that abnormal hemoglobin pigments developed. There was no evidence to suggest that citrated human blood containing this halogenated acetate was different from aliquots of blood serving as controls for the 22-day period required for the in vitro studies; both the test and the control aliquots were maintained at 3 C (37.4 F). However, although animals have been transfused freely with homologous canine blood containing 0.02 M or 0.04 M concentration of the acetate per liter, knowledge on tolerance for it in human subjects is not as yet sufficient to warrant comment upon the possible use of this additive to blood for transfusions in human subjects. Furthermore, the mode of action of this antibacterial agent has not been established, nor is it known whether it has an antiviral effect.

Vagotomy and Antral Resection in the Treatment of Duodenal Ulcer: Results in 514 Patients. J. L. Herrington Jr., L. W. Edwards, K. L. Classen and others. Ann. Surg. 150:499-516 (Sept.) 1959 [Philadelphia].

The authors give an account of their experience with vagotomy and antral resection during the past 12-year period. From January, 1947, through December, 1957, a total of 565 patients were subjected to vagotomy and antral resection for the complications of duodenal ulcer at several surgical clinics in Nashville, Tenn. Exclusive of hospital deaths, patients lost to follow-up, and patients subsequently dying of unrelated causes, a total of 514 patients, or 97% of the total survivors, have now been followed for a minimum of 16 months to a maximum of over 12 years. One hundred seventy-five patients underwent vagotomy, antrectomy, and end-to-end gastroduodenostomy (Billroth 1), whereas 339 patients had vagotomy and antrectomy with a Billroth 2 type of reconstruction. Recurrent ulceration developed in only 2 (0.38%) of the 514 patients.

The excellent and good results among the Billroth 1 and Billroth 2 groups were approximately equal, 91 and 94% respectively. The over-all incidence of the dumping syndrome was approximately equal in both groups. However, no instance of severe dumping was noted in the group undergoing the Billroth 1 reconstruction. Weight losses after operation were slightly less in the Billroth 1 group, as compared with the Billroth 2 group. Vagotomy, antrectomy, and a Billroth 1 reconstruction were the preferred method in cases in which the ulcer could be completely and safely removed. The overall results with the combined procedure of vagotomy and antral resection were quite satisfactory. and the operation appears to offer as much or more protection against recurrent ulceration than does an "adequate" subtotal gastric resection.

Studies on Portal Hypertension: IV. The Clinical and Physiopathologic Significance of Self-Established (Nonsurgical) Portal Systemic Venous Shunts. L. M. Rousselot, A. H. Moreno and W. F. Panke. Ann. Surg. 150:384-412 (Sept.) 1959 [Philadelphia].

The authors report on the occurrence, behavior, and effects of the several types of natural portal-systemic shunting mechanisms as observed in 203 patients, including 135 with cirrhosis of the liver, 15 with different types of extrahepatic obstruction of the portal system, and 53 without pathological conditions in the portal system. This last group and 21 healthy persons served as controls.

Spontaneous diversion of portal blood, either by reversed flow into branches of the portal system or through reopened embryonic channels, was not associated with alleviation of portal hypertension in this series. The rate of hepatic blood flow was not changed by increasing collateralization until esophagogastric varices developed, and only then was it sharply decreased, but diversion of blood through this route did not generally reduce the portal tension. Large embryonic channels connecting the portal and systemic venous circulations were not associated with reductions in portal hypertension. The rate of hepatic blood flow in these cases was decreased. Incidence of bleeding from ruptured varices or severity of the bleeding episodes was not affected by the presence of these large connecting channels. Surgically constructed shunts produced a further decrease in the already diminished hepatic blood flow of patients with esophageal varices. Portal pressure was sharply reduced to the approximate normal range. After a portacaval shunt was surgically established, no back-flow into esophagogastric varices or other collaterals was observed. Hemorrhage from ruptured varices did not recur.

The authors feel that, if their interpretations are correct, the following conclusions may be permissible: 1. Diversion of portal blood from the liver through collaterals and natural shunts has failed to decompress the portal system. 2. Since diversion of portal blood from the liver is an undesirable situation per se, its failure to decompress the portal system is doubly regrettable. 3. When diversion of portal blood occurs through gastroesophageal plexuses, the veins of these plexuses dilate and become tortuous and sacculated. If these varices rupture, a third undesirable side-effect follows, that is, severe gastrointestinal bleeding. 4. A surgically constructed shunt produced a small further decrease in the already diminished hepatic blood flow of patients with esophagogastric varices, but probably it would have produced a sharp decline in patients without these varices who were demonstrated to have normal rates of hepatic blood flow. This situation will have to be considered if a shunt is attempted for the treatment of ascites in patients not having esophagogastric varices. This small further decrease in the presence of an already diminished hepatic blood flow may be responsible for the relative infrequency and mildness of ammonia intoxication observed in these cases.

Etiologic Factors in Polyposis and Carcinoma of the Colon. J. E. Dunphy, W. B. Patterson and M. A. Legg. Ann. Surg. 150:488-498 (Sept.) 1959 [Philadelphia].

This paper explores the question of spontaneous regression of cancer with reference to carcinoma and polyps of the colon on the basis of personal observations and some reports from the literature. Cases are cited which show that diversion of the fecal stream by colostomy is followed on occasion by reduction in the size of distally located carcinomas. Rarely such carcinomas have disappeared completely without other treatment or after supplementary irradiation. There is evidence that preoperative irradiation may improve the 5-year salvage in carcinoma of the rectum. Congenital polyps may regress in the rectum after subtotal colectomy and ileorectal anastomosis. Such regressions have been complete as far as gross identification of polyps are concerned. Histological study, however, may show islands of hyperplastic mucosa. Finally, areas of epithelial hyperplasia have developed in the cheek pouch of the hamster after the heterotransplantation of a carcinoma of the colon.

These facts raise the following questions: 1. May there not be a factor leading to polyposis and carcinogenesis, which is produced or activated by the mucosa of the colon, and which is removed or deactivated by diversion of the fecal stream and partial or subtotal colectomy? 2. Does the colonic mucosa itself produce a factor which stimulates hyperplasia leading to polyposis or carcinogenesis? May not this factor be transplantable with the carcinoma? 3. Whatever the exact mechanism, does not the evidence suggest that diversion of the fecal stream may have a specific antitumor effect and, therefore, be of value in preparing the intestine for cancer surgery? 4. Is the greater frequency of carcinomatous implantation at the suture line in recent years attributable to the fact that, with improved methods for preparing the intestine, preliminary colostomy is seldom used today? 5. Should subtotal colectomy be more widely employed in the treatment of carcinoma or multiple polyps, on the ground that it may eliminate a substance which stimulates the formation of polyps or carcinoma? 6. May not preoperative irradiation affect the growth potential of carcinoma of the colon and rectum, so that it is less likely to be disseminated at the time of operation? While definite answers to the above questions cannot be given, a controlled study of the effects of preliminary colostomy and of preoperative irradiation on carcinoma of the rectum and colon is indicated.

NEUROLOGY & PSYCHIATRY

Serum Lipid and Cholesterol Levels in Cerebrovascular Disease. J. S. Meyer, A. G. Waltz, J. W. Hess and B. Zak. A. M. A. Arch. Neurol. 1:303-311 (Sept.) 1959 [Chicago].

This report is concerned with a statistical analysis of serum cholesterol and lipid determinations in 110 patients admitted to the neurological service of the Receiving Hospital of the City of Detroit with a diagnosis of cerebrovascular disease. The values obtained were compared with those in 2 control groups. No significant difference was found between the mean serum cholesterol or lipid values in 110 patients with cerebrovascular disease and a group of hospitalized patients of comparable age with nonvascular neurological disease. Diabetes mellitus existed in 12.7% of the patients with cerebrovascular disease. The serum lipid or cholesterol values of the patients whose diabetes was under control were not significantly different from those of the rest of the group with cerebrovascular disease uncomplicated by diabetes. Patients with cerebral atherosclerosis involving the vertebral-basilar, internal carotid, or smaller cerebral arteries (i. e., anterior, middle, and posterior cerebral arteries and their branches) did not have mean lipid or cholesterol values that were significantly different from those of healthy men of a mean age of 30 years; but a significantly greater percentage of patients with cerebrovascular disease had elevated serum cholesterol or lipid values. This reflects the tendency of these values to increase with age.

Patients with hypertensive cerebrovascular disease were found to have significant elevations of serum cholesterol and lipid levels, and it is believed that hypertension may be the significant factor in hypercholesteremia and hyperlipemia. The incidence of all types of cerebrovascular disease, including carotid and vertebral-basilar artery insufficiency, was the same in white and Negro groups. Nor was there any racial difference in serum cholesterol or lipid levels. Cerebral symptoms were produced by atherosclerotic involvement of 3 major groups of cerebral vessels. Approximately one-third of the patients showed evidence of disease in the vertebral-basilar artery system, one-third had symptoms due to disease in the carotid arteries, and one-third to disease in the small cerebral vessels (anterior, middle, and posterior cerebral arteries and their branches).

In all types of cerebrovascular disease, the incidence of hypertension was significantly greater than in neurological diseases other than vascular in nature, in spite of the fact that atherosclerotic disease of cerebral vessels commonly manifests symptoms in the absence of hypertension or when a previously elevated blood pressure has fallen to normal levels. Since hypercholesteremia and hyperlipemia probably enhance any tendency toward atherosclerosis of cerebral vessels, the therapeutic use of a low-fat diet in cerebrovascular disease is recommended.

PEDIATRICS

Chylous Ascites and Lymphedema. W. J. Warwick, R. T. Holman, P. G. Quie and R. A. Good. A. M. A. J. Dis. Child. 98:317-329 (Sept.) 1959 [Chicago].

The 5th case of chylous ascites with lymphedema (elephantiasis) to be recorded in the literature is reported. No instances of this rare congenital syndrome have been observed in older patients. The patient reported was female and was born in 1952, after an uneventful pregnancy and spontaneous delivery. The birth weight was 8 lb. and 4 oz. (3.7 kg.); swelling of the entire left leg and right arm and hemangioma lateral to the right eye were observed at the time of delivery. The infant was jaundiced for 4 days after birth. There was no family history of ascites, lymphedema, or hemangiomas. Two children born later have been completely normal. Between the ages of 5 and 45 months the patient was admitted to hospital 9 times for respiratory infections, varying from a "slight cold" to severe pneumonia. While on a low-fat diet, the patient's skin became dry and scaly; her hair became thick, coarse, and sparse; and she developed eczematous lesions over her abdomen, which would come and go without explanation. A marked reversal of these signs occurred after the administration of 10 Gm. of ethyl linoleate. The skin became normal, soft, and smooth, except over the edematous arm and leg, and the hair became fine in texture, silky, and abundant. These changes were still present when the child died in June, 1957.

No significant difference in the content of polyunsaturated acids in the skin of this patient was observed as a result of linoleate supplementation. The main effect of the low-fat diet was a prolonged period of freedom from paracentesis. A defect in the immunological system was suspected; a series of respiratory infections represented a continuous problem during most of the life of this child, and her death was due to overwhelming pneumonia. On autopsy, it was observed that the fat measured only a centimeter in thickness but had a normal appearance. The thoracic cavity was small, and the lungs were compressed because of the extremely high diaphragm. There was no free fluid in the pleural spaces. The abdominal cavity contained 12 liters of sterile chylous material. The entire serosal surface of the abdominal cavity was covered by a shiny white plastic material measuring approximately 6 mm. in thickness. The mesentery of the small intestine could not be separated because of thick, tight adhesions. The entire mucosal surface of the small intestine was covered by collections of fatty material. Dissection of the mesentery failed to reveal lymphatic channels or lymph nodes. A thoracic duct of small caliber was located in the upper thorax but could not be traced below the 10th thoracic vertebra. The cisterna chyli was not found.

Giardiasis, a Cause of Celiac Syndrome. J. A. Cortner. A. M. A. J. Dis. Child. 98:311-316 (Sept.) 1959 [Chicago].

The pathogenicity of Giardia lamblia has been questioned for many years. While the Giardia organisms are usually harmless saprophytic flagellates, it has been thought by many that in heavy infection they may cause an interesting spectrum of diseases. The asymptomatic infection appears at one extreme, and the full-blown celiac syndrome at the other. In between are all degrees of abdominal pain, anorexia, nausea and vomiting, malaise, melena, gallbladder colic, jaundice, malnutrition, and diarrhea. Patients with the intermediate group of diseases may experience reduced fat absorption without clinically evident malnutrition. The author observed 4 children with giardiasis, aged 3 years, 19 months, 10 months, and 22 months, respectively, all suffering from malabsorption of fat similar to that found in the celiac syndrome. Quinacrine had a good effect in all the cases; it eliminated the infection and relieved the resulting symptoms. In one child the improvement was clear-cut and progressive on observations made 8 months after therapy. The other children showed improvement at 2-hour levels with the radioiodine-labled fat absorption tests 5 months after therapy, but further follow-up was impossible. Urine collections were not made during these tests with radioiodine (I^{131}); subsequently urine values proved to afford a more satisfactory method of estimating fat absorption than serum levels. According to the author, giardiasis can be severe enough to interfere with absorption from the duodenum and the upper jejunum, and rarely this can react to such a degree as to produce a picture resembling celiac disease.

Diabetes Mellitus or the Prediabetic State in the Mother and the Neonate: Effect on the Homeostasis of Calcium, Phosphorus, and Some Other Electrolytes in the Neonate on the First Day of Life. I. F. Gittleman, J. B. Pincus, E. Schmertzler and F. Annecchiarico. A. M. A. J. Dis. Child. 98:342-349 (Sept.) 1959 [Chicago].

On the basis of previous research which had shown that the incidence of hypocalcemia on the first day of life was significantly higher in infants born to mothers who had abnormal pregnancies, labor, or both, and that diabetes mellitus in the mother played a prominent role, the authors studied the incidence of hypocalcemia on the first day of life in infants born to diabetic mothers and to mothers who were found to have a prediabetic state during pregnancy. A mother was considered in the prediabetic state when her glucose tolerance curve was diabetic-like in one or more pregnancies. The subjects of the study were divided into 2 groups. The first group consisted of 22 infants born to diabetic mothers whose diabetic state had been recognized over periods varying between 1 and 18 years. All mothers of this group received insulin but no other hormones. All but 2 infants were delivered by cesarean section. The second group contained 36 infants born to mothers who were considered to be in the prediabetic state. The mothers of the second group received no insulin, and the glycosuria was controlled by diet. In this group 23 infants were delivered by cesarean section, and 13 by viae naturales. Mothers who were delivered by cesarean section received dextrose intravenously during the operative procedure. Blood was obtained by venopuncture on the first day of the infant's life, as soon after birth as possible.

The results of the study show that there is an increased incidence of hypocalcemia on the first day of life in infants born to mothers who are diabetic or in the prediabetic state. In infants whose mothers' diabetes is adequately controlled, the incidence of hypocalcemia appears to be related to the mode of delivery (cesarean section). In each of 3 instances in which control of the mother's diabetes was poor, the infant had hypocalcemia on the first day of life. The incidence of hypocalcemia is highest in the offspring of mothers who are in the prediabetic state, indicating that a metabolic disturbance probably played an etiological role in the causation of the hypocalcemia. The mean serum phosphorus value in both the diabetic and the prediabetic series was higher than the mean phosphorus value found in normal infants on the first day of life. However, hyperphosphatemic levels occurred in only 6 of the 22 infants born to diabetic mothers and in 8 out of 36 born to mothers in the prediabetic state. The serum sodium, total carbon dioxide, and chloride levels showed no marked deviations in either group. The serum potassium levels in the diabetic series tended to be higher than normal; this was particularly true in infants who had hypocalcemia. The mean glucose level on the first day of life was significantly higher in the diabetic group when compared with the mean glucose level of normal infants on the first day of life. There was no statistically significant difference between the mean glucose levels of the 2 groups.

Neonatal Hepatitis. R. G. Shorter, A. H. Baggenstoss and G. B. Logan. A. M. A. J. Dis. Child. 98:359-369 (Sept.) 1959 [Chicago].

The clinical and histological records of 8 cases of neonatal hepatitis, 7 of them observed at the Mayo Clinic during the period from 1924 to 1957, are reported. The histological features are contrasted with those seen in the noncirrhotic liver associated with congenital biliary atresia, 40 cases of which were studied. Seven of the 8 patients observed were girls; one was premature according to the birth weight. With the exception of one case in which the mother gave a history of acute hepatitis 3 years before, the family histories were not revealing. Pregnancies had been uneventful in 4 instances; mild toxemia had been present in the last month in one instance and in the last trimester in another; one mother had complained of "itching" during the last month, and another had been vomiting during the first trimester. The most frequent clinical features of neonatal hepatitis—jaundice, abnormal serum concentration of bilirubin, presence of urobilinogen in the stools, bile pigment in the urine, abnormal concentration of hemoglobin in the blood, and hepatomegaly—are similar to those found in association with congenital biliary atresia. There is a lack of any clinical or biochemical specificity for either condition which can facilitate diagnosis and prevent unnecessary surgical exploration of some patients who have neonatal hepatitis.

Histologically, the parenchyma of the liver showed the most dramatic changes in infants with neonatal hepatitis. The degree of necrosis of the hepatic cells was not severe, being of patchy distribution and of lytic type with karyolysis and loss of cell structure. The most obvious and impressive finding was the occurrence of giant cells which were varied in size, the smallest being 2 or 3 times the size of a normal parenchymal cell, whereas the largest was 5 or 6 times as large. The giant cells were multinucleate, the average number of nuclei being 9; their cytoplasm was most commonly eosinophilic. The liver was noncirrhotic in only 3 of the 40 cases of congenital biliary atresia which were also studied. The histological features in these 3 examples were contrastingly different from those seen in neonatal hepatitis. The hepatic architecture was preserved but damaged. Degeneration of hepatic cells varied from mild to severe, being predominantly eosinophilic in type in one case. Giant cells were not seen. The degree of cholestasis was less than that in patients with neonatal hepatitis.

At the time of last inquiry 2 of the 8 infants with neonatal hepatitis had hepatic cirrhosis, and 4 had died within 8 months of the onset of the symptoms. One remained jaundiced 2 months after operation, but the significance of this is obscured by inadvertent damage to the common bile duct at operation. Only one child was apparently in good health. The authors believe that a common histological response to different stimuli may contribute to the difficulty of determining the pathogenesis of neonatal hepatitis.

Diabetes Mellitus and Offspring. F. Thoenes and C. Lenz. Ann. paediat. 193:65-90 (Aug.) 1959 (In German) [Basel, Switzerland].

The authors report on 141 married diabetic women in regard to fertility, pregnancies, and intrauterine and perinatal infant mortality, as well as in regard to birth weight of the newborn infants. The findings are compared with those of a control group of 141 married but metabolically healthy women. The ages of the diabetic women ranged from 22 to 77 years. Results of the study show that the incidence of fertility in women in whom diabetes manifests itself after the reproductive period is 91.8%, whereas only 1 woman in 5 may conceive if diabetes is present during the period of sexual maturity. The incidence of pregnancies in diabetic women is considerably lower than that in healthy women. No appreciable reduction in fetal mortality rate could be observed in this study. In the case of children born to a diabetic mother, every 2nd child dies during the neonatal period at the latest, while every 4th or 5th child of a prediabetic woman dies in utero or perinatally, as compared with every 6th child of a healthy mother. Overweight is encountered in every 2nd and every 3rd newborn infant of a diabetic mother, as compared with every 8th child born to a metabolically healthy woman.

The later the clinical onset of diabetes occurs in the life of a patient, the better are her chances to produce normal, healthy, and viable children. Thus, patients who contract diabetes only after onset of the menopause are deemed to have better results, as far as development of their offspring is concerned, than women whose diabetes has become clinically manifested during the earlier reproductive stage.

Acrodynia. E. Smeby. Nord. med. 62:1233-1234 (Aug. 13) 1959 (In Norwegian) [Stockholm].

Acrodynia, or pink disease, has been observed in almost all parts of the world but most cases are reported from western Europe, especially England, France, and Switzerland. A typical case recently seen in the children's clinic in Bergen, Norway, is described. The disease sets in at an age ranging from 6 months to 4 years, with infection of the upper respiratory tract, moderately increased temperature, and vomiting. Anorexia and a poor general condition follow. The tips of the fingers and toes become erythematous; the erythema gradually spreads. In most cases there is photophobia. Marked hypertonia occurs. The pulse frequency increases, and the blood pressure rises. Tachycardia and hypertension are pathognomonic symptoms. Most authors agree that mercury combinations for medical use can provoke the disease. Mercury in an ointment base of solution can be absorbed by the organism through the whole skin. In cases in which the disease appears after the use of mercurial preparations in therapeutically adequate doses, a hypersensitivity to mercury is assumed to exist. No specific changes characterize the disease. In patients with acrodynia amounts of mercury up to 400 mcg. per liter have been found. The disease should be borne in mind when a small child is treated with medicaments containing mercury.

Exchange Transfusion as a Prophylaxis of Kernicterus in the Premature Newborn Infant. C. Sbraccia and G. Di Piero. Policlinico (sez. med.) 66:314-327 (Aug.) 1959 (In Italian) [Rome].

Exchange transfusion was carried out in 31 hospitalized premature infants with high serum bilirubin level; the babies were deeply jaundiced, but did not have demonstrable mother-newborn incompatibility within the ABO or the Rh system. Jaundice became clinically evident about the 36th hour of life, and the serum bilirubin level was about 28 mg. per 100 cc. on the 5th day of life. Exchange transfusion was performed on the 2nd or the 3rd day of life in 25 instances, on the 7th day in 3, on the 8th day in 1, and on the 10th day in 2. Transfusion of blood was made at the rate of approximately 170 cc. per kilogram of body weight. Speed of exchange was about 200 cc. per hour.

The exchange transfusion was well tolerated by all the patients. The serum bilirubin level ranged from 17 to 44 mg. per 100 cc. before the procedure; these values were reduced by approximately one-half afterward. Transfusion was repeated in only one instance. One infant died after the procedure; intracranial hemorrhage and subtotal atelectasis of both lungs were established on autopsy. Neurological sequelae developed in 2 patients; they had been tardily hospitalized and received exchange transfusion while symptoms of severe involvement of the central nervous system were already present. Indication for exchange transfusion should not be based on the findings of the serum bilirubin level alone; it should also be evaluated in view of the clinical picture.

Early Ambulation in Patients With Acute Rheumatic Fever. E. Nassau and A. Aron. Ann. paediat. 193:101-110 (Aug.) 1959 (In German) [Basel, Switzerland].

The authors made the observation that children with acute rheumatic fever showed great eagerness to leave their beds and to move about as soon as fever subsided and pain disappeared. This observation prompted them to study the effect of early ambulation in 21 children with acute rheumatic fever. The disease was mild in 4 children, moderately mild in 10, and severe in 7. Nineteen patients had experienced their first attacks of rheumatic fever, and 2 had recurrences. The children were treated with cortisone and a proprietary preparation of aminopyrine. An antibiotic drug was given as long as the temperature was elevated. Prophylactic treatment with sulfonamide compounds was started 10 to 14 days after the onset of the disease.

As soon as the children felt well enough for activity, they were permitted to be ambulatory, which usually took place within 9 to 15 days after admission. Laboratory studies were performed routinely each week from the day of admission to the day of discharge, and they were repeated at follow-up examination. The erythrocyte sedimentation rate had already decreased by the time the children were made ambulant, and the vital capacity had increased by 100 to 300 cc. However, the antistreptolysin titer, the C-reactive protein level, and the erythrocyte sedimentation rate were found to be normal only after repeated follow-up examinations. Roentgenologic and electrocardiographic findings were noncontributory in the determination of the condition of these children. The cardiac status remained unchanged from the day when the patients first got up until the time of discharge. Only after months was compensation of cardiac insufficiency observed in 14 of the 21 children, while the symptoms had disappeared in 7. No exacerbations or recurrences of the disease were observed in this group of children.

Thus, it is felt that early ambulation of children with rheumatic fever does not depend on the results of laboratory examinations (antistreptolysin titer, C-reactive protein level, erythrocyte sedimentation rate, and other tests). The restoration to normal of these factors in patients with acute rheumatic fever occurs at the same rate after early ambulation as after long periods of bed rest.

UROLOGY

Oxalosis. V. F. Marshall and M. Horwith. J. Urol. 82:278-284 (Sept.) 1959 [Baltimore].

While urinary calculi composed of calcium oxalate are common, oxalosis is rare. Oxalosis may be defined as the deposition of calcium oxalate crystals in extrarenal tissue as well as in the renal parenchyma and collecting systems of young patients. Deposition of oxalate in the renal parenchyma alone has been termed "idiopathic oxalate nephrocalcinosis." Primary hyperoxaluria signifies only a urinary excretion of oxalate higher than the normal of 20 to 50 mg. in 24 hours. In contrast, secondary hyperoxaluria may be associated with infections, diabetes mellitus, or an unusually high intake of soluble oxalates or precursors, e. g., ascorbic acid. Oxalosis is an advanced stage of some abnormality in the body's manufacture or handling of oxalate. Death results from the renal destruction caused by the deposits, as well as from the well-known secondary effects of urinary calculi. In addition, the deposits in other organs, especially the heart, may have caused a significant alteration in function. Approximately 20 cases of oxalosis have been reported previously.

Two new cases of oxalosis, confirmed at postmortem examination, are reported by the authors. Both of these female patients, aged 18 and 22 years, respectively, died of uremia. In a third case, that of a 23-year-old woman, it is probable that oxalosis is present. Among the diagnostic tools is examination of bone marrow aspirate under polarized light. Renal biopsy should nearly always reveal oxalate nephrocalcinosis, since deposition of calcium oxalate crystals is usually extensive. Failure of the deposits to stain with the von Kossa method should raise the suspicion that they are calcium oxalate rather than calcium phosphate. Examination with polarized light will demonstrate birefringent crystals.

Johnson's incineration test for oxalate was repeatedly negative in the third patient. Two types of crystals were present in the renal parenchyma, the less frequent of which appeared as calcium oxalate monohydrate. A biopsy specimen taken from the sternal marrow appeared histologically normal, but when sections were viewed under polarized light, many small, probably intracellular, birefringent crystals could be noted. A biopsy specimen from asymptomatic, radiographically detected lesions in the left tibia revealed an acute inflammatory reaction with polymorphonuclear leukocytes, but crystals could not be found under polarized light. These bony lesions have remained asymptomatic for more than 6 months, and they are radiographically similar to some reported in cases of oxalosis. The skeleton, including the lamina dura of the teeth, otherwise looks normal. Renal function has been good.

A differentiation of primary hyperoxaluria from oxalosis is suggested. Increased urinary oxalate excretion does not seem to be the major factor in oxalosis. The possibility of primary oxaluria and oxalosis representing analogous conditions of cystinuria and cystinosis is explored. Urinary oxalate excretion was increased by feeding ascorbic acid, glycine, and glycolic acid to the third patient. Administration of sodium benzoate to this patient has had little effect on urinary oxalate excretion. Dietary oxalate is probably not a primary factor. The intimate relationship between glycine and its precursors to oxalic acid is discussed. Although oxalosis is rare, a clarification of this disorder should contribute to the understanding of urinary calculus disease.

Ileal Replacement of the Ureter. P. A. Morales, S. Askari and R. S. Hotchkiss. J. Urol. 82:304-316 (Sept.) 1959 [Baltimore].

The authors present the histories of 9 patients in whom ileal replacement of the ureters was carried out at Bellevue Hospital, New York, during the past 3 years. Four of these patients were encumbered with rubber tubes and bags for at least a year before being completely relieved of them by ileal surgery. Three other patients were able to discontinue catheter drainage, but they still require a collecting appliance for urine excreted through a stoma on the abdominal wall. The operation was carried out in 2 patients who had only one remaining kidney. A complete ileal replacement of the ureter was performed in 3 patients, partial replacement in 2, bilateral partial replacement in 1, combined partial replacement and ileal cystostomy in 2, and complete replacement with ileostomy in 1. One patient died 2 weeks after the operation; of the remaining 8 patients, 6 have been followed for more than a year, and 2 for less than a year.

The use of isolated ileal segments as ureteral substitutes may be considered in patients with postinflammatory or postoperative periureteric fibrosis, with intrinsic or extrinsic tumors, and with accidental or deliberate interruption of ureteral continuity. The operation is, however, not indicated when ureteral continuity can be restored by simpler means. Most urologic surgeons will be able to cope with the technical difficulties involved in the operation, since residents in urologic surgery performed all the operations in this series. The hazard of reabsorption of urinary constituents by the intestinal segment does not appear to be a major problem. As a result of the dynamic peristaltic activity of the ileal segment, urine is in contact with the ileal mucosa only in small amounts and for short intervals. None of the patients in this series manifested any serious electrolytic aberration, although 5 showed slight elevations in serum chloride levels. The possibility exists that, with the accumulation of urine in the bladder, reflux of urine into the ileal segment may promote reabsorption. Inasmuch as it is known that ureteral reflux may be reduced or avoided by frequent voidings, the authors encourage patients with ileal substitution of ureters to micturate at 2-to-3-hour intervals by day and once at night to avoid reabsorption.

Reflux Is Dangerous But Not Always Disastrous: Conservative Treatment Often Effective. D. E. Leuzinger, J. K. Lattimer and C. B. McCoy. J. Urol. 82:294-303 (Sept.) 1959 [Baltimore].

On the pediatric urologic service of the Babies Hospital, New York, a detailed study was made of 148 children with ureteral reflux. One hundred two children had a mechanical obstruction or stricture of the bladder outlet; in 22 the reflux was due to unknown causes; and 24 children had obvious neurogenic bladders. All of those classified as having neurogenic bladders also showed other neurological defects, and the majority had meningoceles. Forty-two additional cases were reviewed, but were not included because of insufficient follow-up data. The incidence of ureteral reflux among all children admitted for urologic disorders was 4.6% (190 cases out of 4,093 new pediatric urologic admissions, from 1937 to 1957).

The review of the 190 children with ureteral reflux suggested the following generalizations concerning this condition: 1. Untreated ureteral reflux tended to be deleterious to the kidney involved and should make it difficult to eradicate urinary infections in such a kidney. Successful treatment of ureterovesical reflux turned out to be easier than expected. 2. Conservative treatment was surprisingly effective. Even severe degrees of ureteral reflux were often markedly improved by conservative measures to relieve obstruction and to decrease the resistance of the bladder outlet. Two-thirds of the patients treated were greatly benefited. 3. The efficacy of simple urethral dilatation with sounds was surprising. The majority of the patients whose condition improved did so following conservative methods of increasing the caliber of the bladder neck and urethra. 4. The large dilated bladder appeared to afford a "cushion" which protected the ureter and kidney pelvis from severer dilatation and may have made the cure of reflux easier.

The ordinary signs and symptoms of urinary infection, in the form of fever and pyuria, were by far the commonest in patients with reflux. Reflux and urinary tract dilatation were more severe in males than in females, although the over-all incidence of reflux was the same in both sexes. All the patients who died, or failed to improve, entered the hospital with severe dilatation of the urinary tract and elevation of the serum nonprotein nitrogen level. On the other hand, death occurred among only 10 children out of 70 who entered the hospital with reflux plus an elevation of the nonprotein nitrogen level. Failure of the azotemia to resolve after drainage was an ominous sign. Although conservative therapy was surprisingly successful, studies are now in progress to determine at the time of admission those patients who will do well and those who will require more drastic treatment.

Cancer of Bladder and Its Treatment. M. Andersen and J. Glenert. Ugesk. laeger 121:1322-1325 (Aug. 27) 1959 (In Danish) [Copenhagen].

In 57 of the 60 cases of cancer of the bladder in the personal material reported on, in 48 men and 12 women, aged from 28 to 87 years, hematuria was the direct cause of admission. The diagnosis, verified histologically in 51 cases and at autopsy in 4 other cases, was papillomatous carcinoma, with invasion of the muscular coat in 35 cases. In 29 patients radical treatment was possible. Twenty-one of these patients were followed up for 1½ years or more; 15 have been free from recurrence for from 1 to 7½ years, average time, 3½ years. Cancer of the bladder is a grave disease with unfavorable prognosis in the advanced stages. With early diagnosis and treatment the chance for recovery is favorable. Every patient with hematuria should be examined more closely without delay. Cystoscopy supplemented by biopsy gives the exact diagnosis. Classification according to histological localization (mucosa, submucosa, muscular coat, perivascular tissue, metastases) seems to afford the best basis for prognosis and therapeutic considerations. Treatment is predominantly surgical. Transurethral electrocoagulation is carried out on smaller, superficial tumors; suprapubic electrocoagulation or electroresection, on larger or multiple superficial tumors. If possible, resection of the bladder is performed in the case of tumors invading the mucosa. Cystectomy and extended cystectomy are large interventions with high primary mortality and poor late prognosis. In recent years the results of treatment have been somewhat improved by a combination of surgical intervention and implantation of radiotantalum.

Male Subfertility and the Childless Marriage. L. S. Scott. Scottish M. J. 4:354-358 (July-Aug.) 1959 [Glasgow].

For many years it was believed that, as long as the husband was not impotent, a barren marriage implied sterility of his wife. We now know that the male is as often at fault as his partner; of 1,011 husbands seen at the male infertility clinic of the Western Infirmary, Glasgow, in the past 2 years, 40% were undoubtedly subfertile, and 1 in 10 was sterile. Desire for children is stronger in women than in men, and it is the wife who is usually first to seek advice. A childless marriage requires investigation of both partners, but the husband should be examined first. Examination includes a general examination to rule out endocrine disorders; examination of the penis for congenital deformities; palpation of the prostate, vesicles, vasa, and epididymides; and a careful appraisal of the size and consistency of the testes. It has been shown that 65% of patients with small testes are subfertile, and 20% sterile.

Seminal analysis is the most important investigation. The seminal specimen is collected in a dry glass container. Condom specimens are valueless as motility is destroyed. Patients are instructed to abstain from intercourse for 3 days before the test, and the specimen should be examined within 2 hours of ejaculation. The volume of the ejaculate should be between 2 and 5 ml. Motility should be estimated by microscopic examination on a warmed slide. It should reveal purposeful movement of at least 75% of the sperms 2 hours after emission. Morphology is the most difficult factor to estimate, as there is as yet no proof that abnormal morphology may lead to abnormal pregnancies or congenital abnormalities. Seminal counts are expressed in millions per milliliter, and normal values are believed to lie between 20 and 300. Testicular biopsy is indicated when 2 consecutive seminal analyses reveal complete absence of sperms. It has no value in patients with low seminal counts, but, if azoospermia is present, histological evidence of normal maturation of sperms suggests a block in the conducting system which may be amenable to surgery. On the other hand, early histological evidence of maturation arrest or tubular atrophy—neither of which respond satisfactorily to treatment—can prevent years of worthless and costly drug therapy.

Daily intercourse for 5 successive days causes a 50% drop in the sperm count, but increasing the period of continence to 6 or more days merely results in an increased ejaculate with decreased motility; the optimum interval appears to be 3 or 4 days. Mumps in childhood in 164 of the men studied by the author had no effect on fertility. Epididymitis was not caused by gonococci in the 5 patients observed by the author, but 3 of them were subfertile and 2 were sterile. Of 2 patients with a history of genital tuberculosis, 1 was subfertile and 1 sterile. Herniotomy in childhood had produced traumatic atrophy of the testes in 14 men, of whom 10 were either subfertile or sterile. Maldescended testes are frequently maldeveloped and commonly associated with subfertility. Hydrocele and varicocele may depress spermatogenesis by raising the intrascrotal temperature. The surgical treatment of varicocele, hydrocele, and obstructive azoospermia holds some promise. Drug therapy has been disappointing in male sterility, but the occasional use of testosterone may be indicated.

Carcinoid Tumor of the Testis Occurring in a Systic Teratoma of the Testis. S. W. Berkheiser. J. Urol. 82:352-355 (Sept.) 1959 [Baltimore].

A 54-year-old man had had an enlarged left testis since birth. This was asymptomatic until one year prior to admission when gradual painful enlargement was noted. The pain was relieved slightly by a truss support. More noticeable enlargement and a dull dragging pain in the left testis occurred during the week before admission. The clinical findings were thought to be indicative of a hydrocele. At operation, however, the left testis was found to be greatly enlarged, firm, and indurated. Since neoplastic involvement was suspected, orchiectomy was performed. When pathological examination revealed a cystic teratoma (teratocarcinoma) with a carcinoid component, radical lymph node dissection with complete removal of the spermatic cord and vas deferens was advised. This was accomplished 2 weeks after the initial orchiectomy.

On pathological examination it was found that the testis was replaced by a cystic tumor, which measured 8 by 6.5 by 6 cm. The lesion was composed of numerous cysts and cyst-like spaces. Small firm nodules having the consistency of cartilage and bone were noted in the wall of the various cysts. Step-block sections throughout the tumor were examined. The fibrous stroma was thin and delicate, resulting in a definite organoid appearance considered typical of carcinoid tumors. Specific staining disclosed numerous black, argentaffin granules within the cytoplasm. Groups of typical carcinoid cells were present throughout the wall of many of the cysts. Most were lined by tall columnar cells suggestive of gastrointestinal tract origin.

Earlier reports on functioning carcinoid tumors have indicated that these neoplasms function in the same manner as endocrine tumors as a result of serotonin secretion. The demonstration of abnormal amounts of 5-hydroxy-3-indole acetic acid in the urine is of great aid in confirming the diagnosis. Unfortunately in the present case, as well as in the only similar case reported by Simon, McDonald, and Culp in 1954, these studies were not obtained prior to surgical removal of the tumor. Neither of these cases, however, demonstrated the clinical features of diarrhea, pain, asthma, or cardiovascular complications which may be associated with functioning carcinoids. The origin of carcinoid tumors within teratoid tumors of the testis is not known. Simon, McDonald, and Culp noted that the tissue, in relation to which the carcinoid tumor arose, could not be identified definitely, but appeared to resemble respiratory tract derivatives. In the present case the close association of carcinoid elements with gastrointestinal-type mucosa and structures was more in favor of a gastrointestinal origin. The reaction of the carcinoid cells to silver staining is likewise more suggestive of gastrointestinal origin than of respiratory derivatives.

OPHTHALMOLOGY

Hypophysectomy as a Therapeutical Method for Proliferative Diabetic Retinopathy. S. Vannas, C. A. Hernberg and G. af Björkesten. A. M. A. Arch. Ophth. 62:370-380 (Sept.) 1959 [Chicago].

Proliferative diabetic retinopathy, in which recurrent hemorrhages lead to incurable blindness, accompanied by painful secondary glaucoma, occurs as a complication of the labile juvenile diabetes that is difficult to control with insulin. Clinical investigations and experimental studies have indicated that the development of diabetic retinopathy is associated with adrenal cortical hyperfunction, which may be the cause of the retinopathy. It is possible that both diabetes and diabetic retinopathy are due to the abnormal functioning of the hypophysis, in which case the adrenal cortical hyperfunction is a secondary phenomenon. Recent experiments point to somatotropin of the pituitary as responsible for the diabetogenic action. In either case, hypophysectomy may have a beneficial effect on diabetic retinopathy.

The authors report ophthalmological observations on 10 patients with diabetic retinopathy, on whom hypophysectomy was performed. The patients had had the labile form of diabetes for from 10 to 18 years. One eye was practically blind in most of the patients, and vision in the better eye was seriously threatened by the proliferative changes. The optic nerve of the worse eye was severed near the chiasm for reasons of technique except in 2 cases. Five patients showed postoperatively a temporal defect also in the visual field of the better eye. The time that elapsed after operation ranged from 3 months to 2 years and 10 months. After hypophysectomy the need for insulin diminished to approximately one-half. Proteinuria disappeared in 3 patients. Central vision in the better eye remained unchanged or improved somewhat in 7 patients. In 3 patients vision deteriorated postoperatively because of new hemorrhages.

Typical changes were observed in the eyegrounds after hypophysectomy. Dilatation of venules and capillaries tended to regress, and microaneurysms and macroaneurysms seemed to disappear; the same applied to the newly formed vessels. Existing hemorrhages were absorbed, and the bleeding tendency diminished. Even a massive hemorrhage could be absorbed and dry up into shiny patterns and crystals. Waxy exudates and cotton-wool patches tended to disappear. The rate of proliferation diminished. The strands that developed after recurrent hemorrhages were dry-looking and situated deep in the retina, and, if newly formed vessels were absent, no shrinkage was observed. Favorable changes notwithstanding, the authors emphasize that the risk involved in hypophysectomy is considerable, and attention must be paid during postoperative care both to the hormone-electrolyte balance and to the danger of infections. Although the patients have an extremely gloomy prognosis, it is not yet possible to make a final evaluation of hypophysectomy as a therapeutic method against proliferative diabetic retinopathy.

Vitamin B_{12} and Herpes Zoster Ophthalmicus. J. M. Heaton. Brit. J. Ophth. 43:438-439 (July) 1959 [London].

Vitamin B_{12} is quite often given to patients with herpes zoster ophthalmicus, as it has been reported to reduce the severity of the disease and the incidence of complications. In order to ascertain whether there is any evidence of vitamin B_{12} deficiency, 16 patients with herpes zoster ophthalmicus were examined and a history was taken, chiefly to make sure that they had not been given vitamin B_{12} recently in any form. Sixteen controls of the same sex and approximately the same age (± 4 years) were also examined. The serum vitamin B_{12} concentrations were measured by microbiological assay, with the green alga, Euglena gracilis var. bacillaris, as test organism. No evidence of vitamin B_{12} deficiency was found in the 16 patients with herpes zoster ophthalmicus. Probably vitamin B_{12} has no effect in reducing the severity of this disease or its complications.

Ataxia-Telangiectasia. J. L. Smith and D. G. Cogan. A. M. A. Arch. Ophth. 62:364-369 (Sept.) 1959 [Chicago].

The authors present a detailed history of an 18-year-old Negro woman who had ataxia-telangiectasia. Although ocular symptoms are prominent in this form of cerebellar ataxia, the authors state that this is the first case of ataxia-telangiectasia that has been reported in the ophthalmological literature. The ocular abnormalities are (1) a curious defect in executing voluntary ocular movements and inability to maintain full excursions of the eyes and (2) the presence of prominent conjunctival vessels, which have been so marked as to be called telangiectasia. The vision, pupils, and fundi are usually normal, as is the electroencephalogram. The patient presented showed, in addition to the typical features, the following aspects not previously noted: 1. Hers was the first case in the Negro race and the second oldest in chronological age. 2. The spinal fluid protein level was elevated. 3. Vertical nystagmus was present, and the optokinetic nystagmus response (nystagmus produced by looking at a moving object) was absent. The pneumoencephalographic evidence of cerebellar atrophy noted in this case has been reported in other cases and appears to deserve further emphasis. The ophthalmological signs of ataxia-telangiectasia are of prime importance in its recognition.

THERAPEUTICS

Treatment of Pulmonary Tuberculosis with Isoniazid and Pyrazinamide: Experience in 114 Cases. M. J. Small. Dis. Chest 36:265-279 (Sept.) 1959 [Chicago].

One hundred fourteen patients who had originally been treated with either pyrazinamide (PZA) or isoniazid (INH), and whose tubercle bacilli were susceptible to INH, received a combined PZA-INH treatment for periods of 1 to 25 months. With the exception of 3 women, all the patients were men, between 21 and 76 years of age. The diagnosis of pulmonary tuberculosis was bacteriologically confirmed in all except 3 patients, in whom previous therapy of less than 2 weeks' duration, or minimal extent of the lesion, made the confirmation impossible. All the patients had a Bromsulphalein (BSP) retention not exceeding 7% in the 45 minutes prior to the administration of PZA. The daily doses were 300 mg. of INH and 3 mg. of PZA (later reduced to 1.5 mg. for some patients). If and when there was a significant elevation in the BSP retention, confirmed by prompt repetition of the test, the administration of PZA was discontinued.

Roentgenologic evaluation of the results was made at the 4th month of treatment and was limited to 58 patients with far-advanced or moderately advanced tuberculosis. There was marked improvement in 22 patients, moderate improvement in 17, slight improvement in 10, and no change in 8; one patient was worse. In 11 patients there was persistence of cavitation, although the bacteriological status had become negative. Of the 8 patients who showed no roentgenologic change, 3 suffered from chronic fibroid involvement, and 5 had large cavities. Five of these 8 patients had a negative bacteriological status and returned to normal activities. Bacteriological evaluation, also at the 4th month of treatment, was applied to 55 patients for whom the diagnosis of far-advanced or moderately advanced tuberculosis had been confirmed bacteriologically, and whose bacilli were shown to be susceptible to INH. Fifty-one (93%) of these patients had their bacteriological status converted to negative. The 4 patients (7%) who retained a positive status had become resistant to INH after 2 months of treatment.

Of the 114 patients receiving the PZA-INH therapy, 22 (19%) experienced side-reactions in the form of hepatic disorders. In 16 patients the therapy had to be discontinued because of an asymptomatic rise in BSP retention. There was evidence of hepatitis, together with abnormal liver function tests, in 3 patients; elevation of serum alkaline phosphatase value in one; and anorexia, together with a high BSP retention and nausea, in another. One patient became jaundiced after 6 weeks and died within 48 hours. As he had undergone surgical procedures and multiple blood transfusions, it is doubtful that the PZA hepatotoxicity was the cause of death. It is advisable that the combined PZA-INH therapy be limited to cases in which it is possible to have frequent hepatic function tests and laboratory indexes for early detection of PZA toxicity.

1314 Th or Thioamide of Alpha-Ethyl-Isonicotinic Acid in the Treatment of Cavitary Tuberculosis. P. Véran, C. Moigneteau, R. Trichereau and N. Rist. Rev. tuberc. 23:533-569 (May-June) 1959 (In French) [Paris].

Alpha-ethyl-thioisonicotinamide (1314 Th) was used in treating (1) 38 patients with long-standing cavitary tuberculosis, in whom the bacilli had become resistant to isoniazid and streptomycin, and (2) 17 patients with recent tuberculosis. The immediate results in the long-standing cases were often dramatic. The late results, on the other hand, depended to a great extent on whether or not the development of drug resistance could be prevented by using, in addition, another medicament to which the bacilli were still fully sensitive. A combination of 1314 Th and streptomycin proved to be as effective as the standard combination of isoniazid and streptomycin in the limited number of cases of recent tuberculosis in this series. No resistance to streptomycin appeared when 1314 Th was given in association with it, and vice versa. 1314 Th, therefore, deserves a place beside isoniazid, which is still the principal antituberculous medicament, in treatments of attack. Further experience will show whether 1314 Th can advantageously be used to replace streptomycin or PAS in combination with isoniazid.

Signs of drug toxicity are not observed when 1314 Th is given in doses of either 0.5 to 1.0 Gm. a day by mouth or 1.0 to 1.5 Gm. a day in suppositories. Episodes of gastric intolerance occur much less often now that a way has been found to improve the coating of the tablets. These episodes can be suppressed almost entirely by giving the drug rectally instead of orally. Assays of the level of active 1314 Th in the serum after rectal administration indicate that absorption is as good when the drug is given by this route as when it is given orally.

The minimum useful dose of 1314 Th has still to be determined. The maximum dose that can be tolerated (0.75 to 1.0 Gm. orally; 1.0 to 1.5 Gm. in suppositories) should undoubtedly be prescribed when isoniazid is not given, and also when patients are treated with drug combinations in which 1314 Th is the principal bactericidal medicament. It is possible, however, that in combination with isoniazid the necessary and adequate dose may be of the order of 0.5 Gm. The problem of tolerance would, in this case, rarely arise in treatments of attack, and 1314 Th might be widely used in the treatment of patients at home.

Treatment of Malignant Tumors of the Extremities by Perfusion with Chemotherapeutic Agents. E. T. Krementz, O. Creech Jr., R. F. Ryan and J. Wickstrom. J. Bone & Joint Surg. 41:977-987 (Sept.) 1959 [*Boston*].

The authors used a new technique in treating 37 patients with malignant tumors, 17 of whom had malignant melanoma, 17 some type of sarcoma, and 3 primary or metastatic carcinoma, all involving the extremities. This technique included intra-arterial administration of the chemotherapeutic agents as well as continuous recirculation of the drug-containing perfusate with the aid of a pump oxygenator. Perfusion of the lower extremity was accomplished through the external iliac, common femoral, or superficial femoral vessels, depending on the location of the tumor. In the upper extremity, the subclavian, axillary, or brachial vessels were used.

Of the 17 patients with malignant melanoma, 13 were treated for palliation. Three of these patients died; 2 of them had the local tumor controlled but died of distant metastases; the third patient died as a result of an excessive dose of phenylalanine mustard with inadequate isolation of the extremity. Among the 10 living patients treated for palliation, 3 have recurrent disease, and in 7 the disease is considered quiescent. In 4 of the 17 patients with melanoma, perfusion was performed as an adjunct to surgical excision. In 3 of these the disease has been controlled; in 1 patient a local recurrence occurred, but after excision of the diseased area, no further activity was noted. These patients were perfused with phenylalanine mustard alone, except for 2 perfusions with a combination of phenylalanine mustard and triethylene thiophosphoramide and 1 perfusion with triethylene thiophosphoramide. In the 17 patients with sarcoma of the extremities, 20 perfusions were performed. The chemotherapeutic agent was nitrogen mustard in 10 perfusions, phenylalanine mustard in 6, both phenylalanine mustard and triethylene thiophosphoramide in 2, and actinomycin D and 5-fluorouracil in 1 perfusion each. Of 4 patients in whom perfusion was used as an adjunct to surgical excision, one died; in another the lesion recurred but is quiescent after retreatment; in the remaining 2 patients the disease seems to be controlled. Of 13 of the 17 patients who were treated for palliation, 5 died. Among the living patients, 4 have had varying degrees of regression of their tumors with subsequent recurrence, while in 1 patient the lesion is quiescent and in 3 the lesions are controlled.

In one patient with an epidermoid carcinoma of the thumb, in whom perfusion was carried out 2 weeks prior to an anticipated amputation of the thumb, regression of the tumor occurred. The patient has had no evidence of recurrence at follow-up, 14 months after treatment. Another patient with metastatic adenocarcinoma in the tibia from the kidney showed some evidence of local improvement after perfusion. In a 13-year-old girl with multiple bony metastases of all extremities, some regression occurred in the perfused extremity, but the patient's family refused further procedure and the girl died 2 months after the original treatment. Local and systemic complications have been minimal after isolated perfusion of the extremities.

Anticoagulant Therapy with Phenindione: Clinical Analysis of 101 Cases. A. Buzzi, O. Fustinoni and B. Carbajal. Prensa méd. argent. 46:687-692 (March 20) 1959 (In Spanish) [Buenos Aires].

The course and prognosis of intravascular thrombotic processes have greatly improved with the preventive and therapeutic use of anticoagulants. Between 1956 and 1958, 101 patients suffering from different cardiovascular diseases were treated with the anticoagulant phenindione at the Institute of Semiology of the Hospital de Clínicas, in Buenos Aires, and in the authors' private practice. There were 38 patients with coronary insufficiency, 25 with venous thrombosis, 18 with auricular fibrillation, 13 with arteriosclerosis obliterans of the lower extremities, 3 with acute arterial embolism, 2 with cerebral thrombosis, and 2 with chronic cor pulmonale. Phenindione was administered in the form of 50-mg. and 25-mg. tablets. Most patients received an initial dose of 200 mg. the first day, followed by 100 mg. the second and third days. From the fourth day on a maintenance dose of 75 mg. was the rule. This dose was later reduced to 50 mg. or was increased, according to the course of the cardiovascular condition. In a few cases it was necessary to seek a faster effect, and the doses were 300 mg. the first day, 200 mg. the second, and 100 mg. the third, followed by the maintenance dose. Whenever the daily dose was 50 mg. or higher, it was divided into 2 doses, taken at 12-hour intervals. Low doses of 25 mg. were given to patients with advanced cardiac or renal insufficiency.

In 80% of the patients the results were satisfactory. In those with acute thrombophlebitis the course of the disease was invariably favorable. As to coronary insufficiency, approximately half of the patients suffering from retrosternal pain resistant to analgesics and vasodilators obtained relief. Within 24 hours from the beginning of the therapy, a reduction in the prothrombin time could be observed. The maximal effect was obtained within 36 hours. Elimination of phenindione takes place within 36 to 48 hours after interruption of the treatment, and within 72 hours all effects of the drug disappear. Eight patients in this series had hemorrhage. To 6 of them it was necessary to administer vitamin K in order to normalize the prothrombin concentration.

The response to phenindione therapy was comparatively uniform in each patient, although it varied with the person. Only in 4 patients who received prolonged treatment was it necessary to increase the doses. The results obtained in this series indicate that phenindione is an anticoagulant of rapid absorption and elimination, which produces more constant results, with less danger of causing sudden changes in blood prothrombin, than bishydroxycoumarin (Dicumarol) and its derivatives.

A Comparative Study of Four Prothrombinopenic Anticoagulant Drugs: II. Clinical Study. T. Rodman, C. S. Ryan, B. H. Pastor and others. Am. J. Med. 27:415-423 (Sept.) 1959 [New York].

A preliminary appraisal of 4 commonly used and representative prothrombinopenic drugs—bishydroxycoumarin (Dicumarol), warfarin (Prothromadin), phenindione (Hedulin), and diphenadione (Dipaxin)—had provided information about the action of these agents which seemed to have practical clinical implications. The studies described in this paper are concerned with an evaluation of these 4 anticoagulants over a period of 14 months in 287 patients requiring anticoagulant therapy. Somewhat better control was achieved with bishydroxycoumarin and diphenadione than with phenindione and warfarin. The differences were statistically significant but not great. Satisfactory control of prothrombin activity was achieved in the majority of the patients with all 4 drugs. There was relatively wide variation in dosage requirements in the same patient from day to day and among patients receiving the same preparation. This variation was less with bishydroxycoumarin and diphenadione than with phenindione and warfarin. An induction schedule, which consisted of a large single loading dose followed by a small maintenance dose, was found to be desirable and safe. By means of such a program the prothrombin activity in the majority of patients (82%) was brought into the therapeutic range within 40 hours of the initial dose with all 4 drugs. This program also facilitated the early establishment of a stable maintenance dose.

PATHOLOGY

Melanin Pigmentation of the Endocervix: A Visceral neurogenetic Discussion. M. Cid. An. cir. 24:63-78 (March-June) 1959 (In Spanish) [Rosario, Argentina].

Melanin pigmentation of the endocervical symplasm is exceptional and has no visceral parallel. Among 108 specimens obtained from gynecologic operations and examined by the author during 1957-1958, 5 contained endocervical pigmentation, which amounted to an unexpected 3.6%. Two cases, which are believed to be the first in the medical literature, are reported here. The first patient was 40 years old and was operated on for a myoma. There were cysts near the external opening of the uterine cervix, and a bluish area of undetermined contour on the posterior surface in the middle third of the duct. Under microscopic examination this area measured 10.4 mm. in length. It was formed by isolated, independent foci, with the central focus extending farther and deeper among the glands than the others. In a slightly fibrous stroma the structural elements were interwoven with melanocytes. The pigmented cells were undoubtedly differentiated stromatic cells, for they had the same distribution and nuclear characteristics.

The second specimen studied was removed from a 43-year-old patient. Examination of the specimen showed interstitial multiple fibromas, uterine and ovarian endometriosis, and follicular cysts. On the posterior wall of the endocervix, approximately 2 cm. from the external opening, there was a bluish area of rather well-defined contour and resembling the blue nevi of the skin. Microscopically, a pigmented area was seen, measuring 8 mm. in length and 3 mm. in width. It was fusiform, slightly elevated, nodular, and separated from the surface by a thin layer of normally colored tissue. The nodule structure was fibrous. Histologically, 4 different sectors were perceived. Sector A showed a loose, reticulated structure where the melanogenesis, although light, had produced elements identical with the elements in the other sectors. In sector B, superficial and also fibrous, there were marked hyalinosis and pigmentation, bipolar and epithelioid cells. Sector C, under sector B, was the most extensive and most strongly pigmented area; it had a fibrous structure without hyalinization, bipolar or fusiform cells, and a few epithelioid cells. Sector D was small and presented a loose, fasciculated structure, less fibrous than the others but composed of the same fusiform and epithelioid elements. This sector contained an additional small area of loose structure and different characteristics. The trichromic cells showed numerous parallel traces of collagen, crisscrossed and ramified, which were easily interpreted as a neuromatous, amyelinic structure.

In both cases reported, the endocervical stroma was formed by cells which had very uniform nuclei, with cytoplasms barely discernible among the collagenous fibers. The endocervical stroma was an extensive symplasm, or a syncytium of Schwann's sheath, masked by fibrosis and partly pigmented. As shown by the histological analysis of these 2 specimens, Schwann's sheath is capable of originating both achromic and pigmented cells.

Hydatid Cyst of the Thymus (First World Case[?]). V. A. Ugon, S. Piovano and D. Tomalino. Torax 8:48-52 (March) 1959 (In Spanish) [Montevideo].

This case of primary hydatid cyst of the thymus is believed by the authors to be the first reported in the medical literature. The patient, a 14-year-old boy, was hospitalized because of roentgenologic findings during a school mass chest examination. He had been operated on 5 years before because of a hydatid cyst of the left lung. The physical examination was unrevealing. The roentgenograms showed a left hilar growth, with a darker, round image in the center and another growth higher up in contact with the mediastinum. Fluoroscopic and electrocardiographic examinations showed no cardiac abnormalities. Other tests were also negative. The absence of symptoms and a comparison with previous roentgenologic signs led to discarding the possibility of a vascular malformation. Given the past occurrence of a hydatid cyst, the probability of mediastinal hydatidosis was admitted. A posterolateral thoracotomy on the left was performed with the patient under anesthesia given by tracheal intubation. The pulmonary walls were loosely adhesive to the mediastinum and were easily liberated. A growth, the size of a hen's egg, was found implanted on a hypertrophic thymus, and in the upper pulmonary lobule there was a soft growth, the size of a nut. The thymus, with its growth, and the pulmonary nodule were removed; the mediastinal pleura was closed; and closed pleural drainage was instituted. The postoperative course was uneventful, and the patient left the hospital 2 weeks later in good condition.

The thymus removed from this boy weighed 55 Gm. and measured 80 by 55 by 22 mm. The pulmonary nodule was ovoid, reddish, and elastic, with a 34-mm. diameter. The macroscopic and microscopic examinations showed that (1) the larger specimen was actually a thymus; (2) the thymus was very well preserved for the patient's age, probably because interference by the parasite may have arrested the usual involution; (3) the pulmonary nodule corresponded to a hydatid cyst developed in the subcortical parenchyma and encased in a fine fibrosclerotic adventitia; and (4) the hydatid membrane showed the characteristic structure of a chitinous membrane with lesions of hyaline degeneration.

Studies on Human Leukemia. L. Dmochowski, C. E. Grey, J. A. Sykes and others. Proc. Soc. Exper. Biol. & Med. 101:686-690 (Aug.-Sept.) 1959 [Utica, N. Y.].

Studies on the relationship of viruses to tumors led to discoveries through the employment of such methods as use of newborn animals, electron microscopy of ultrathin sections of different tumors, and tissue culture. The authors report here electron-microscope studies on ultrathin sections of lymph nodes from 6 patients with acute lymphatic leukemia, 1 with acute and 1 with chronic monocytic leukemia, 1 with acute myeloid leukemia, 2 with lymphosarcoma, and 1 with Hodgkin's disease. Virus particles, of approximately 900 angstrom units in diameter, were observed in cells of lymph nodes from 3 patients with acute lymphatic leukemia, 1 with acute myeloid leukemia, and 1 with lymphosarcoma. Similar studies of sections of lymph nodes from 5 nonleukemic patients failed to reveal virus particles. Cytopathogenic changes were observed in cells of lymph nodes, grown in vitro, from 15 of 24 patients with leukemia and lymphosarcoma. Cells of lymph nodes, grown in vitro, from 4 nonleukemic patients did not show changes observed in lymph nodes from leukemic patients during a similar number of passages. Cell-free extracts of lymph nodes from 8 patients induced changes in monkey-kidney-cell cultures, which could be serially transmitted. These changes were not seen in similar cultures treated with extract of a nonleukemic lymph node. Extracts of leukemic lymph nodes which induced changes in monkey-kidney-cell cultures did not have a similar effect on human embryo cultures.

Cell-free extracts of biopsy material from leukemic and lymphomatous lymph nodes and fluids from monkey-kidney-cell cultures treated with these extracts did not show leukemia-inducing activity in mice. It is of particular interest that in one patient with lymphosarcoma not only were virus particles observed in ultrathin sections of the biopsy specimens but also similar virus particles were found in cells from the same specimen, grown in vitro, for 6 sequential passages during which cytopathogenic changes had been observed.

BOOK REVIEWS

Arthritis: General Principles, Physical Medicine, Rehabilitation. Edited by Edward W. Lowman, M.D., Associate Professor of Physical Medicine and Rehabilitation, New York University College of Medicine, New York. With twenty-four collaborators. Foreword by Howard A. Rusk, M.D. Cloth. $9.50. Pp. 292, with 134 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. &. A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1959.

Problems resulting from the presence of chronic forms of rheumatic disease often go far beyond matters which directly concern diagnosticians and clinical therapeutists. The well-rounded rheumatologist should have more than an acquaintanceship with symptoms, physical findings, and laboratory tests. Patients with rheumatic ailments not only need medication and reconstructive operations but they need guidance in regard to occupational and recreational activities. Psychological adjustments must be made with family members, business colleagues, neighbors, and friends. Jobs need to be changed. Crippled patients must learn to overcome disabilities and must be taught to eat, dress, walk, and get about. The patient with a chronic rheumatic disease must be helped and taught to help himself. The job is complex and the techniques involved are only now being evolved. Proper care of such patients requires the help not only of physicians but of psychiatrists, psychologists, social workers, physical therapists, brace makers, and many other specialists. Arthritics are numerous and their numbers are increasing.

The editor and his collaborators have produced an interesting book, which presents the general nature of this complex problem in an interesting and valuable manner. Brief chapters are devoted to the differential diagnosis of rheumatic diseases, anatomy, pathology, and traditional medical therapy. Subsequent chapters discuss many facets of the problems of treating arthritic patients, such as testing ranges of joint motions, useful programs of physical therapy that can be carried out in the home, and occupational therapy.

Physicians working with arthritic patients should find much of interest in the sections on materials and methods of splinting, gait training, and the use of crutches. Newly developed techniques of rehabilitation involving the use of self-help devices and of training disabled homemakers are adequately presented. Shoes, shoe corrections, postural training, the function of visiting nurses in treatment of rheumatic diseases, the philosophy of using mobile physical therapy units, and the role of the voluntary health agencies in supporting and improving the lot of arthritic patients are discussed.

Basic Surgery. Edited by Leslie Oliver, M.D., B.S., F.R.C.S., Neurosurgeon, West London Hospital and Medical School, London. Cloth. $26.50. Pp. 1359, with 680 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; H. K. Lewis & Co., Ltd., 136 Gower St., London, W. C. 1, England, 1959.

It is difficult to evaluate this book because, while a tremendous amount of surgical material is excellently presented, one encounters ideas and omissions which would not be acceptable to American teachers of undergraduate medical students. For example, in the discussion of aids to diagnosis of appendicitis it is stated that "the white cell count may mislead even an experienced clinician and is probably best ignored." It is true that there is wide variability in this symptom, but most appendicitis cases follow a fairly regular pattern. A few patients with the disease well developed have normal counts and others have very high counts. In omitting the subject of the cell count the authors fail to present what is known about appendicitis. There are other instances where British treatment methods differ from those in use here. The American student, already overwhelmed with the great mass of clinical detail, had best learn one way thoroughly at first.

In spite of these minor criticisms the book is interesting. The format is excellent, the type is good, and the divisions of subject matter are easy to follow. Every section shows the hand of an expert. The text is ably supported by excellent diagrams and illustrations. The section on genitourinary surgery by Page has an authoritative approach, and it is surprising to those used to specialization to find later in the book his chapter on the breast. Flavell presents the natural history and other features of intrathoracic disease in a capable manner. His masterly use of statistics adds force to his thesis. The section on neurosurgery by Oliver is commendable, as are Bonnin's chapters on orthopedics. The subject of infections of the hand, however, deserves more than the two and one-half pages allotted to it. This book is not recommended for American medical students.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

EMPLOYMENT AND PREGNANCY

To the Editor:—*A company, employing women for office and cafeteria work, desires to establish a policy about when their employees should take maternity leave. Some women have insisted that they be allowed to work almost to their expected day of delivery and the company feels that there is need for mutual protective rules for itself and the women.*

William H. Liesenbein, M.D.,
Poughkeepsie, N. Y.

Answer.—An employer has a valid right to require pregnant employees to take a maternity leave within a reasonable time prior to the anticipated date of delivery. Under the Workmen's Compensation laws, which are in effect in many states, an employer may be held responsible for compensation to employees who are injured in the course of their employment. Consequently, an employer would be concerned about an employee who might be prone to accidents because of her gravid status.

Answer.—The company should establish a policy for employees to take maternity leave. The employee should not work after the sixth calendar month of the pregnancy and should not resume her work until the sixth week post partum. In exceptional situations, where the woman works in an individual office and has sedentary activities, private rest facilities, and no transportation problems, employment might be continued until six weeks prior to the expected date of confinement.

PSITTACOSIS IN PET BIRDS

To the Editor:—*How does one make a diagnosis of psittacosis from parakeet droppings, and what is the treatment of birds with this disease?*

R. O. Howard, M.D., Wichita, Kan.

Answer.—Efforts to isolate the virus from the droppings of parakeets or other birds are seldom successful because of the dilution factor and massive bacterial flora which cannot be suppressed by antibiotics in quantities that will not kill the virus. Diagnosis of psittacosis in birds often is confirmed by the isolation of the virus from the blood or sputum of the patient who contracts the illness from the bird. Repeated attempts to accomplish this isolation may be necessary, and, if the patient has been treated with antibiotics, isolation of the virus is even more difficult. Any material suspected of containing the psittacosis virus must be regarded as potentially infectious and dangerous to handle, unless proper precautions are observed. Psittacosis cannot be diagnosed, with certainty, by clinical or gross anatomic examination of the patient. Impression smears of lesions from the serosa of the air sacs, liver, heart, and intestines of suspect birds, properly stained by the Giemsa or Macchiavello methods, reveal the intracellular or extracellular elementary bodies. Material in which the virus can be demonstrated microscopically is excellent for isolation of the agent by inoculation of mice. Attempts to propagate the virus directly from infected birds in the yolk sac of embryonating eggs are not always successful.

The complement-fixation test is valuable in detecting psittacosis in man and some birds. A rising titer in paired serum specimens, taken 7 to 10 days apart, can be considered presumptive evidence of active infection. Recently a nonspecific antigen for psittacosis diagnosis in man has been used. It consists of a killed suspension of Bacterium anitratum. Lymphogranuloma venereum antigen may be used for the complement-fixation test in the event a reliable, specific antigen is not available. The direct complement-fixation test demonstrates antibodies in man and psittacine birds and, occasionally, in pigeons, while the indirect complement-fixation test is used with the serums of turkeys, ducks, pheasants, and usually pigeons. The virus frequently has been isolated from human beings and birds who showed negative results of complement-fixation tests.

Psittacosis can be controlled or eliminated in parakeets by chemotherapy with tetracycline compounds given in medicated feed or by injections. The method of treatment as given in annex 13, page 81, *World Health Organization Technical Report Series 169 (1959), Joint WHO-FAO Expert Committee on Zoonoses, Second Report*, published by the World Health Organization, Geneva, Switzerland, is as follows: "Acute psittacosis in parakeets has been controlled by oral administration of aureomycin in the feed in doses of not less than 100 milligrams per kilogram. Interrupted treatment providing medicated feed for not less than thirty days and if necessary, repeated, has ultimately eliminated one carrier state in a parakeet aviary as provided by sampling of the F_1 to F_4 generations.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

. . . The drug is conveniently administered orally, by feeding hulled millet seeds impregnated with 0.5 mg. of aureomycin per gram of feed. An interrupted schedule of offering the medicated feed—from three to five days of medicated feed, followed by regular feed for one or two days, over a period of a total of 30 days of drug intake—has brought about complete, but not always immediate, cures. Success has been achieved only by conscientious aviculturists who maintain high standards of sanitation and isolation. . . ."

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ACUTE ANXIETY AND SLEEP

To the Editor:—*A 50-year-old college professor who performs an active schedule of teaching and research has had, for five years, progressive attacks of the following symptom complex. After a moderately hard day's work he will retire to bed and, at the exact moment of beginning sleep, he awakes with a sensation of a complete cardiac and respiratory arrest. This sensation is intensified when the day has been one of greater than usual physical exertion or emotional tension. These episodes always cause the professor to panic and they may recur four or five times before restful sleep is attained. Medicaments given for sedation often stop the symptoms and usually decrease their severity. The phenomenon always occurs when an attempt is made to sleep during the day. Could this be due to hyperactive adrenal function? What is the diagnosis and treatment?*

D. W. Kittredge Jr., M.D., Flagstaff, Ariz.

Answer.—It is not possible to determine the physiological events associated with the symptoms described. This is a disabling set of symptoms, and hospital observation is necessary to determine what actually happens. It is possible that some type of respiratory tract obstruction occurs with relaxation: for example, the base of the tongue may occlude the larynx, as often occurs in patients under deep anesthesia. This man may, unknowingly, hyperventilate. The symptoms could be entirely of a psychogenic nature, in which case psychotherapy would be indicated.

Answer.—It is reasonably certain that the patient's symptoms are manifestations of acute anxiety. The symptoms of other patients having identical complaints have been permanently relieved by intensive psychotherapy. Hyperactivity of the adrenals is one of the physiological components in attacks of acute anxiety.

TESTS FOR TOXIC REACTIONS TO TRANQUILIZERS

To the Editor:—*When chlorpromazine and similar drugs are given to patients with mental illness on a long-term basis, what laboratory tests, if any, should be done to detect complications such as agranulocytosis and liver damage? Some physicians depend on physical signs and symptoms, others do blood counts for the first three months, and recently a white blood cell count and a transaminase test to be done monthly was recommended.*

M.D., Michigan.

Answer.—It should be noted that the problem of complication of agranulocytosis is probably not the same as that of jaundice. Agranulocytosis has been carefully studied for its relationship to a number of these drugs in the past and is known to occur at any time during the course of treatment. It may develop after a few doses of the drug or after many months or even a year or more of exposure. Leukocyte counts should be done at intervals of about two weeks, if one is to be certain of making the diagnosis early. Leukopenia frequently precedes the agranulocytosis, so these counts might be spaced at intervals of one month. Jaundice due to chlorpromazine and related drugs usually develops within five days to three months after the treatment is started. The simplest and most satisfactory way to detect jaundice is by determination of bilirubin in the urine. Tests for this should be done weekly during the first two months and every other week for the third month. The possibility of jaundice developing after this time is slight. Jaundice due to drugs similar to chlorpromazine is possible but much less likely.

PRIMARY ANKLE EDEMA

To the Editor:—*What laboratory studies should be done in order to be certain that ankle edema occurring in a healthy adult woman is chronic lymphedema? What treatment other than with elastic stockings and diuretics may be of benefit?*

William Y. Rial, M.D., Swarthmore, Pa.

Answer.—If the patient is a healthy woman, no more than a urinalysis is indicated. If there is to be further study, one should rule out (1) congestive heart disease, (2) nephrosis, (3) pelvic tumor, and (4) deep phlebitis, by means of the following laboratory studies: determination of circulation time, urinalysis for albumin content (over 500 mg. per 100 cc.) and albumin:globulin ratio, venogram, (either percutaneous or with an injection of dye), and x-ray studies, if indicated by pelvic or rectal examination (gastrointestinal study or intravenous pyelogram, or both). If 1, 2, and 3 are ruled out, the chronic lymphedema is either lymphedema praecox (Milroy's disease) or is secondary to chronic thrombophlebitis. If the distinction is unclear, the venogram will distinguish between the two, but this differentiation is often academic.

In addition to use of an elastic support and treatment with hydrochlorothiazide, the patient should seek employment that does not require standing; use a hassock when resting; elevate the foot of the bed 6 in., unless the swelling subsides overnight with a flat bed; and take a diet to which no salt is added. During chlorothiazide therapy the serum potassium level should be determined after two weeks and again in two or three months, because 43% of patients develop a serum potassium level below 3.5 mg.% with this therapy. When this occurs, administration of supplementary potassium chloride is necessary. A pint of orange juice ingested daily may prevent hypopotassemia.

CLEAN TOILET FIXTURES

To the Editor:—*Is there available a toilet seat equipped with ultraviolet light or a disinfecting device that is practical and effective? I want to install one in my office washroom for the benefit of patients, especially women, asked to furnish a sample of urine.*

Joseph D. Thomas, M.D., Denmark, S. C.

Answer.—Ultraviolet irradiation of toilet seats or similar devices does not have any significant advantage over scrupulous cleaning of the toilet fixtures. Ultraviolet light provides superficial surface disinfection, and the contamination of most concern here would be by small masses of feces or mucus. These are far better removed by frequent scrubbing with soap and water or an effective disinfectant, or both. I do not believe that a specially designed toilet seat is necessary, and it may discourage the use of more effective hygienic measures.

CHLOROQUINE

To the Editor:—*What have been the results from administration of chloroquine to patients with rheumatoid arthritis?*

M.D., Wisconsin.

Answer.—Chloroquine is one of several antimalarial drugs which are believed to influence favorably the course of rheumatoid arthritis and similar diseases. In the United States two double-blind studies have shown it to have an antirheumatic effect. There has also been favorable comment from British rheumatologists. My personal experience is in accord with these claims. Chloroquine effects a response slowly, often taking one to three months before any is apparent, and the response may continue to increase for prolonged periods during its administration. There are many side-effects but few are dangerous. They include anorexia, with weight loss; leukopenia; deposits of pigment in the cornea; and skin rashes. To date no deaths have been reported, and the toxicity appears to subside on withdrawal of the drug. It takes many years before the place of an antirheumatic in the treatment of a life-long and highly variable disease such as rheumatoid arthritis can be realistically assessed. It is too early to make an authoritative statement about the degree of improvement and the percentage of patients favorably affected by chloroquine. A report from Canada indicates that certain patients can tolerate treatment with the drug for periods up to five years.

RECURRENT VITREOUS HEMORRHAGE

To the Editor:—*A 75-year-old woman has had recurrent vitreous hemorrhages of the left eye which appear to come from the superior temporal retinal vein. She has minimal evidence of arteriosclerosis and her blood pressure is normal. A fair degree of vision is regained between hemorrhages. Could this be related to a temporal arteritis on the same side? If so, would resection of a portion of the temporal artery be indicated?*

M.D., Virginia.

Answer.—In temporal arteritis, the temporal artery on the side of the defective vision is thickened, nodular, tender, and tortuous. Loss of vision is usually permanent, and there is no vitreous hemorrhage, although retinal hemorrhages may occur. If the patient is not treated the headache increases gradually to the point of mental confusion, and bilateral blindness can result. The management of the patient described would be to seal the defective vessel, if the area can be located, with use of the new retinal light coagulator. Resection of a portion of temporal artery should also be helpful.

STEROID THERAPY FOR MUMPS

To the Editor:—*A man suffering from mumps requested tablets "like his 2-year-old daughter was given for mumps by a pediatrician." The tablets were a corticosteroid preparation and they apparently caused the child's swelling to go down in 36 hours. I recently read Dr. Walter Modell's book, "The Relief of Symptoms," and noted this use of steroid therapy. Would I be justified in prescribing this for an adult male with mumps or secondary orchitis? If so, please give dosage.*

M.D., Illinois.

Answer.—The corticosteroids have an anti-inflammatory action which can affect all types of infections (including viral infections such as mumps). This anti-inflammatory action will cause, in many cases, a reduction of pain, swelling, and fever. It has been conclusively demonstrated that both viral and bacterial infections in animals may be made worse, due to a decrease of localization of the inflammatory reaction, by administration of corticosteroids. There is sufficient clinical evidence to show that this is duplicated in humans. Consequently, treatment with corticosteroids should not be given unless the infecting organism is known and an antibacterial agent is given at the time to combat the infection. There is no effective agent with antagonistic action to the mumps virus, and so there is a hazard connected with corticosteroid treatment.

There are certain areas of the body where an inflammatory reaction can cause damage by pressure if the swelling becomes too severe; infections in the limited space of the calvarium would be one example and orchitis another; for the patient with severe orchitis the best treatment would be with corticosteroids. Dosage would be 100 to 200 mg. of cortisone a day, with the amount decreased rapidly as soon as the extreme swelling started to disappear.

CAUSES OF ADHESIVE ARACHNOIDITIS

To the Editor:—*What are the causes of adhesive arachnoiditis occurring in association with internal hydrocephalus?* *M.D., Ohio.*

Answer.—The causes of adhesive arachnoiditis are as follows: 1. Subarachnoid hemorrhage—the blood causes adhesions, which prevent the proper flow of cerebrospinal fluid. 2. Trauma—trauma could cause a hemorrhage in the subarachnoid space or a tear in the arachnoid membrane. The tear would permit cerebrospinal fluid to enter the subdural space and would permit the arachnoid membrane to become adherent to the pia mater and obliterate the subarachnoid space. 3. Infection—the arachnoid membrane would be the membrane most affected by a bacterial meningitis, and it is possible that adhesions would form between the arachnoid and the pia mater. Regardless of the etiological mechanism of adhesive arachnoiditis, the absorption of cerebrospinal fluid would be hindered; if more cerebrospinal fluid is produced than is absorbed, internal hydrocephalus can develop.

RADIOACTIVE GOLD

To the Editor:—*It was reported that John Foster Dulles received an injection of radioactive gold to reinforce x-ray treatments. Is treatment with radioactive gold used for patients with cancer? What research has been done on this?*

C. G. Krupp, M.D., Grand Rapids, Mich.

Answer.—Radioactive gold (Au^{198}) emits both beta and gamma rays and has a half-life of 65 hours. It is frequently used in radiation therapy and is supplied by several pharmaceutical firms. When the colloidal form is injected into the peritoneal or pleural space it is deposited on the serosa; thus radiation is given to these surfaces. The beta rays, which supply most of the radiation, do not penetrate to a depth of more than several millimeters. Radioactive colloids have been found useful in the palliative management of patients with recurrent pleural and peritoneal malignant effusions. The incidence of effective control is reported to be 50%.

Reference

Beierwaltes, W. H., and others: Clinical Use of Radioisotopes, Philadelphia, W. B. Saunders Company, 1957, pp. 257-272.

FLUOROSCOPY OF THE WELL CHILD

To the Editor:—*Patients have stated that fluoroscopy was routinely performed on their children when they were examined by physicians. Is this a proper procedure?*

Jack L. Webb, M.D., Farmersville, Texas.

Answer.—It is unwise to expose children regularly to fluoroscopy for purposes of routine examination. Roentgen radiation should be used only when vitally needed. The limits of safety for radiation may be approached without adequate reason and later roentgen radiation may thereby become hazardous, for it is cumulative in its effect.

TRANSPORTATION OF BACTERIA

To the Editor:—*Much has been written about the hazard of wound contamination during the operative care of a patient. In an effort to minimize this possibility a hospital forbids anyone from entering the operating suite without change to a scrub suit. In addition, nurses and doctors must put on a gown over their scrub clothes to leave the operating room floor for another part of the hospital. The patients, however, are brought directly to the operating rooms in their beds, without transfer to a cart either before entering or when leaving the operating room for the recovery room. Could this serve as a source of contamination since the bed probably is thoroughly exposed to bacteria from all sources such as bedpans, clothing of visitors, and others?*

M.D., Illinois.

Answer.—The practice of bringing patients to the operating rooms in unsterile beds could be a significant factor but the relative importance of this route of contamination in comparison with other routes is difficult to evaluate. The patient and members of the surgical team are constantly emitting bacteria into the air and secondary dissemination takes place by air currents and movements of personnel. The spread of organisms can be reduced but it cannot be totally prevented. There should be adequate ventilation to prevent accumulation of bacteria in the air and to do this a ventilation system must provide adequate inflow of sterile air for dilution of the bacterial concentration in the air. A positive air pressure in the operating room will prevent the flow of bacteria from adjacent unsterile areas or by air currents through doorways.

HYDRARTHROSIS

To the Editor:—*A 27-year-old man, born in Iraq, developed painless hydrarthrosis of both knees. Roentgenograms of the knee joints are normal except for the presence of fluid. Eighty milliliters of clear, straw-colored viscous fluid was aspirated from the joints. No other joints are affected. Previous aspirations and injections of hydrocortisone have given only temporary relief. Diagnosis and suggestion as to treatment are requested.*

Meier Lichtenstein, M.D., San Francisco.

Answer.—Bilateral hydrarthrosis of the knees may be due to any one of several factors. In order of probability they are (1) atypical onset of rheumatoid arthritis, (2) allergic arthritis, (3) infectious arthritis, (4) intermittent hydrarthrosis, and (5) systemic lupus erythematosus. The following studies are indicated for differentiation: complete blood count, determination of erythrocyte sedimentation rate, sheep cell agglutination or bentonite flocculation test, L. E. cell preparation, study of synovial fluid (smear, cell count, culture, and mucin precipitate), and synovial biopsy if necessary. When the diagnosis has been established, treatment should be directed accordingly. Aspiration and intra-articular instillation of hydrocortisone are valuable adjuncts to therapy in all the conditions listed. Initially this would be done every three to seven days and then at lengthened intervals as the synovitis is brought under control.

MANAGEMENT OF A CHONDROSARCOMA

To the Editor:—*A 22-year-old man has had a tumor of the right thigh for the past year. It has slowly enlarged, now is a hard mass about the greater trochanter of the right femur, and measures 9 by 4 in. by external examination. The radiologist reported findings consistent with a chondrosarcoma, and specimens obtained by biopsy were examined by two pathologists who concurred in the diagnosis of chondrosarcoma. It was considered to be a tumor of low-grade malignancy. The patient has no complaints other than the size of the tumor. Roentgenographic examination of pelvis and chest and other studies did not indicate metastatic spread of the neoplasm. What is the surgical management of this problem?*

R. C. Speckhals, M.D., Faribault, Minn.

Answer.—There are several alternatives. It might be possible to resect the entire proximal end of the femur with the tumor (en bloc) and substitute an Austin-Moore type prosthesis or a Jewett nail and bone graft. If this is done, there may be local recurrence necessitating interpelviabdominal amputation later. Another alternative is massive irradiation with use of cobalt-60 or 1,000-kv. x-ray. This has been successful in achieving no more than temporary regression and growth restraint. The most appropriate management would be an interpelviabdominal amputation, since the grade of malignant activity has been properly established and the location of the tumor appears to make it unsuitable for a disarticulation of the joint. The patient would have a 95% chance of operation survival and a 35% chance of five-year survival.

PROPER USE OF POSTAL SERVICES

To the Editor:—*Is it legal for a physician certified for medical practice in one state to send medicine or prescriptions, or both, to a patient in another state?*

M.D., Indiana.

Answer.—The answer cannot be concise because the circumstances are variable. A physician must be licensed to practice medicine in order to legally prescribe for a patient. If he writes a prescription in one state for a patient in another state, and he is not licensed in the other state, the doctor's position might be one of practicing medicine in the distant state without the qualification of a state license. There may be federal or state statutes or postal regulations for control of interstate mailing of drugs and prescriptions. These would have to be known and, where applicable, would influence an answer. A possible charge of malpractice must be considered. In some instances there could be continued use of a prescription without examination of the patient. There is always the danger of patient self-diagnosis without adequate knowledge, background, or experience. If self-diagnosis by the patient is relied on, the physician assumes the responsibility. Thus there are many practical reasons which make prescribing by mail or sending medicines through the mail inadvisable.

TRANSFUSION WITH INCOMPATIBLE BLOOD

To the Editor:—*In cases of donor-recipient blood-mixing incompatibility, what is the largest amount of blood that has been given a patient who has survived the resulting reaction?*

Alan A. Kane, M.D., Brooklyn, N. Y.

Answer.—Bordley reported five patients who recovered after receiving incompatible blood. The average amount received was 314 cc. Ten patients receiving an average of 564 cc. died. Patients receiving less than 350 cc. recovered and those receiving more than 540 cc. died.

Daniels and co-workers reported seven deaths in patients who received transfusions of 500 ml. or more of incompatible blood; of six patients who survived three had received 500 ml. and three 350 ml. or less. The case fatality rate was 70% in 10 patients who received 500 ml. of blood or more and 0% in 3 who received 350 ml. or less. Survival prognosis may depend on the general condition of the patient. Patients having poor health or anemia are likely to have a more severe hemolytic reaction, and if a patient should have damaged kidneys such a reaction is often lethal.

References

Bordley, J., III: Reactions Following Transfusion of Blood, with Urinary Suppression and Uremia, Arch. Int. Med. **47:** 288-315 (Feb.) 1931.

Daniels, W. B.; Leonard, B. W.; and Holtzman, S.: Renal Insufficiency Following Transfusion: Report of 13 Cases, J. A. M. A. **116:**1208-1215 (March 22) 1941.

"IRRITABLE BOWEL" SYNDROME

To the Editor:—*A 47-year-old man has had a mucous discharge from the anus for four years. The discharge is watery and seems to occur when he has emotional flare-ups. At times there is uncontrolled soiling of his underclothing. He has been examined by several physicians, including a proctologist. No abnormalities were found by examination or by various laboratory tests. Administration of antispasmodic and sedative medicaments have given only temporary relief for three to seven days. He has had no weight loss or other symptoms, except for feeling tense and nervous. What are the diagnostic possibilities and recommendations for treatment?*

George R. Farrell, M.D., San Diego, Calif.

Answer.—The history and findings support the diagnosis of "irritable bowel" syndrome, a term more applicable than "mucous colitis" or "spastic colon" syndrome. This condition is not associated with evidence of an inflammatory process involving the large intestine. Discomfort in the abdomen and the lower lumbar or sacral region may be a part of the symptomatology and commonly is increased during periods of stress, anxiety, or tension. The frequent watery and mucous discharge and soiling of clothing probably are a result of rectal discharges secondary to a partially incompetent anal sphincter. Some improvement may be gained by exercises designed to strengthen the sphincteric muscle. Cleansing of the anal area with water after defecation and the local application of witch hazel from impregnated disks may help.

PNEUMOPERITONEUM

To the Editor:—*To what extent is artificial pneumoperitoneum being used in the treatment of patients with pulmonary tuberculosis?*

A. B. Dickey, M.D., Madisonville, Ky.

Answer.—In 1948, the Committee on Non-Surgical and Drug Therapy of the American College of Chest Physicians sent to 57 physicians (32 different states) 10 representative case reports of patients having pulmonary tuberculosis and a reproduction of the patient's chest x-ray films along with a questionnaire. That year only a few physicians recommended pneumoperitoneum; in 1953, when the same group of cases was sent to 100 physicians, 35% recommended pneumoperitoneum. In 1958, the same 10 cases were sent to 100 physicians and about 12% recommended pneumoperitoneum. Pneumoperitoneum had considerable prominence between 1948 and 1953 but lost much of it (the opinion of the 100 physicians queried) by 1958.

Antituberculosis drug therapy and resectional operative procedures have had a relatively short existence. Tuberculosis is a disease for which a mode of patient management must be observed over long periods before it can be truly conclusive. Five years is too short a time and 10 years is not long enough. Pneumoperitoneum is not an obsolete procedure and may regain popularity. All physicians should know its value.

The book "Pneumoperitoneum Treatment," written by Dr. Banyai, gives the history and an appraisal of the treatment.

PURIFICATION OF SWIMMING POOL WATER

To the Editor:—*Several patients have asked about the safety and effectiveness of the ultraviolet ray-sterilizing process used for home swimming pools. It has been stated that chlorination need not be used with the ultraviolet ray. Is such a claim valid?*

Charles H. Finney, M.D., Phoenix, Ariz.

Answer.—Ultraviolet light in the wave-length range from 2,000 to 3,000 units is bactericidal if the organisms are exposed to a sufficient amount of ultraviolet energy. The problem of assuring that this is done, continuously and to all of the water, has not been solved by the equipment on the market. In general the public health agencies have not approved ultraviolet light as a means of disinfection for public water supplies or public swimming pools.

Ultraviolet light has no residual disinfecting effect and contamination added by bathers to a pool would not be treated until the water is returned to the ultraviolet unit. This is a serious drawback of ultraviolet disinfection as compared to chlorine, which has a residual action.

PUBLIC HEALTH AND SWIMMING POOLS

To the Editor:—*Are any recommendations or regulations concerned with the operation or construction of swimming and wading pools for public use?*

Robert J. Blough, M.D., Deshler, Ohio.

Answer.—The American Public Health Association has a volume entitled, "Swimming Pools and Other Public Bathing Places: Recommended Practice for Design, Equipment and Operation of," ed. 10, 1957. It is 60 pages long and its price is $1.00. Write to APHA, 1790 Broadway, New York 19.

WASHINGTON NEWS

Congress Meets . .
Chemical Additives . .
Private Insurance Progress . .
Fluoridation . .
Tax Proposal . .
Health Expenditures . .

CONGRESS MEETS FOR CRUCIAL SESSION

The 86th Congress began its second and final session with an unusual number of bills affecting the medical profession among the major measures on Capitol Hill.

Foremost was the controversial Forand bill before the House Ways and Means Committee. This measure, opposed by the administration, the American Medical Association, and many other groups, would extend the social security program to include financing of partial health care for old-age and elderly survivors'-disability beneficiaries. The committee last year held hearings on the bill but took no action. No hearings have been slated yet on this bill, although it appeared likely the committee would chart sessions on the social security program as a whole. Backers, including organized labor, have pledged a drive to win support of the bill this year.

The Keogh-Simpson bill to encourage self-employed persons to invest in retirement plans was slated to be one of the first bills taken up by the Senate Finance Committee. The House approved it last year. The measure, backed by organizations of self-employed persons such as farmers, businessmen, lawyers, and physicians would offer self-employed persons tax treatment on savings for retirement similar to that now given salaried persons.

Various bills have been introduced for federal aid for building of medical schools, and a special advisory group to the Public Health Service has recommended a 10-year program of matching federal grants. The administration was expected to propose some type of assistance program for medical education early in the session.

Other legislation would:

1. Liberalize the social security program for the permanently and totally disabled by removing the 50-year age requirement before benefits can be received;
2. Provide a 50-million-dollar annual program for international medical research cooperation;
3. Broaden the Food and Drug Administration's powers to guard the public against use of possible dangerous chemical additives in food and cosmetics;
4. Require compulsory labeling of hazardous household substances;
5. Appropriate sums for the federal government's various medical activities, including the research of the National Institutes of Health and the Defense Department's Medicare program for treating civilian dependents of military personnel in civilian hospitals.

CHEMICAL ADDITIVES

Commissioner George P. Larrick of the Food and Drug Administration declared he knew of no substance now used in food that would be barred if Congress armed the agency with powers to revoke already existing permits for use of food additives.

The administration has urged Congress to eliminate the so-called grandfather clause in pure food legislation that binds the FDA to past approvals for use of chemical additives in food even though later rules might bar new applications.

The administration position, and the recent rejection of an application for use of the sex hormone stilbestrol in grain feed, led to some speculation that the FDA planned to reverse some already granted permits if Congress agreed to revoke the grandfather clause.

However, Larrick and Arthur S. Flemming, Secretary of Health, Education, and Welfare, made it clear that there was no such intention. Flemming explained that under the law it was mandatory for the agency to reject the new application for stilbestrol. The drug, used for the fattening of cattle, has been shown to induce cancer in test animals (not cattle), but no residues have been discovered in meat.

A recent amendment forbids the use of any chemical additive "found to induce" cancer in animal or man. Although HEW favors the legislation, Flemming said he believes there should be a bill to allow use of stilbestrol because it does not show up in meat.

As for dropping the grandfather clause, he said, "If we conclude that a new application for use of a chemical or drug that leaves a residue in human food should be turned down because it has been demonstrated that it will induce cancer in the diet of an animal, we should be able to proceed promptly to revoke all outstanding approvals for the use of the chemical or drug in question."

PRIVATE HEALTH INSURANCE ACHIEVEMENTS

An industry spokesman declared that health insurance companies are demonstrating effectively their capacity for providing medical, surgical, and hospital coverage for older persons.

Robert R. Neal, general manager of the Health Insurance Association of America, noted there have been drives in Congress to finance partial health care for the elderly through the social security system. Neal said this would result in the federal government's taking over a large and important area which has been the responsibility of the enterprise system.

(*Continued on next page*)

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Lown, B., and Levine, S. A.: Current Concepts in Digitalis Therapy, Boston, Little, Brown & Company, 1954, p. 23, par. 2.

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"Obviously, the establishment of federal administrative machinery to operate health insurance programs could possibly be the forerunner of government intervention in other fields of insurance," he said in a speech before the American Association of University Teachers of Insurance.

"The basic issue, then, is whether the voluntary system, which has achieved so much for so many millions of people in so short a span of years, is to be permitted to demonstrate that it can and will continue to serve the public interest with greater effectiveness and at lower cost than can the cumbersome, rigid, and expensive methods which would be employed by those who advocate governmental intervention," he asserted.

FLUORIDATION OF WATER SUPPLIES

The Public Health Service warned that the trend is away from new fluoridation programs for community water supplies, noting that for the past three years the increase in the number of persons drinking fluoridated water has lagged substantially behind the growth in urban population.

During this period, the agency said, the number of persons not benefiting from fluoridated water has increased from 73,500,000 to 76,800,000.

"If this trend continues, a rapidly increasing number of children in this country will be deprived of safe, effective, and inexpensive protection against one of the most widespread diseases—tooth decay," said PHS.

The agency noted that "virtually all scientific and professional health organizations with competence in this field, including the American Dental Association and the American Medical Association, have urged the fluoridation of public water supplies."

Since 1956 the number of communities taking positive action on fluoridation has declined steadily, according to PHS, dropping to a low of 97 this year compared with 233 in 1956.

TAX PROPOSAL AIDS CLINIC PHYSICIANS

The Internal Revenue Service issued a proposed regulation that would encourage physicians who are officers of qualified clinics to invest money in retirement plans.

Briefly, the proposal, which may become final, would treat certain types of clinics as "corporations" under the tax laws. This would mean that officers of the clinic would be entitled to deduct as business expenses funds set aside for retirement programs for members of the clinic.

Self-employed physicians would continue to be barred from such tax treatment on their individual savings for retirement, although a measure pending in Congress would allow them and other self-employed persons such as farmers and lawyers to defer taxes on such savings.

The IRS regulation was a follow-up of a 1954 U. S. court of appeals decision upholding the claimed deductibility of a pension plan of a group of physicians operating the Western Montana Clinic in Missoula, Mont.

Under the IRS proposal, a clinic must at least have associates and the objective of carrying on business for a profit to qualify. Other characteristics would be continuity of life, i. e., that a member of the organization who withdraws could not cause its dissolution; centralization of management; liability for corporate debts limited to corporate property; and free transferability of interests.

MEDICAMENT-APPLIANCE COSTS MORE THAN PHYSICIANS' BILLS

The government reported that Americans paid more for medicaments and appliances than for physician's bills in 1958, for the first time in history. Physicians collected about 4.3 billion dollars in fees from patients in 1958, 62 million dollars less than was spent for medicaments and such appliances as eyeglasses and braces.

According to Social Security Administration statistics, the nation's private health cost rose to a peak 16.4 billion dollars, an increase of almost 1 billion over 1957, representing $95.65 for each person in the country.

Privately financed hospital bills in 1958 totaled 5.1 billion dollars, of which 2.6 billion dollars was covered by insurance. Insurance paid for about 1.3 billion dollars of the physicians' bills.

The figures did not include health expenditures by all levels of government, estimated at nearly 5 billion dollars in 1958.

Of the 5.1 billion dollars of privately-financed hospital bills in 1958, nearly 1.7 billion dollars was for dentists' services and 769 million dollars more for the services of osteopaths, chiropractors, private nurses, and other professional medical personnel. Nursing homes collected about 200 million dollars.

MISCELLANY

The National Institutes of Health requested the cooperation of physicians who have patients with moderate to severe hypertension that is either primary or renal in origin. The major interests of a study being conducted by the section on experimental therapeutics at the NIH clinical center are the development of improved therapeutic agents and investigation of alterations of metabolism of various vasoactive amines such as norepinephrine and serotonin, by means of administration of agents which are enzyme inhibitors. Physicians interested in referring patients for study should write or telephone Dr. Louis Gillespie Jr., Section on Experimental Therapeutics, National Heart Institute, Bethesda, Md. (OLiver 6-4000).

The National Institutes of Health issued a call for children with solid tumors, tumor types of particular interest being Wilms's tumors, neuroblastomas, rhabdomyosarcoma, mesenchymal mixed tumors; and lymphomas. It is hoped that some of the newer agents active in animal tumors will improve on the present results from chemotherapy, said NIH. Physicians interested in referring patients should write or telephone Dr. Clyde O. Brindley, Senior Investigator, National Cancer Institute, Bethesda 14, Md. (OLiver 6-4000).

The U. S. Public Health Service reported that the radiostrontium (Sr^{90}) level in the Nation's major rivers and lakes continues "far below" danger levels. The tests, taken weekly at 51 stations on 17 major watercourses, are part of a stream pollution survey and the over-all PHS check on whether radiation levels are rising as a result of nuclear tests.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 *North Dearborn St., Chicago 10,* Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Northwest Society for Clinical Research, *Seattle, Jan. 9. Dr. John* R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" *Street, Anchorage, Alaska, Chairman.*

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, *Roosevelt Hotel, New Orleans,* Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, North Carolina Chapter, Hotel Barringer, Charlotte, N. C., Feb. 26-27. For information write Dr. Alexander Webb Jr., 201 Bryan Bldg., Cameron Village, Raleigh, N. C.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, *Statler Hilton, Boston,* Feb. 29-Mar. 3. *For information* write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. *Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz.,* Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, *Deauville Hotel,* Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on *Fundamental* Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, *Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St.,* Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chi Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secret Treasurer.

American Academy of General Practice, Philadelphia, Mar. 18 Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, M Executive Director.

American Association for the History of Medicine, Inc., Charle S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Instit Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadm Colorado Springs, Colo., Mar. 21-23. *For information* write: Dr. H. P Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Portl Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H. P Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, Ne Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. o Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Treasu

American Laryngological Association, Deauville Hotel, Miami Beac Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Tec nology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Socie Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Stew Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Fla. Mar. 13-14. *Dr. Lawrence R. Boies, University Hospital,* Minneap 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauv Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barber Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, Mont real, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N.Y. *Executive Assistant.*

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Ri Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory Uni versity, Atlanta 22, Ga., Secretary.

Intermountain Pediatric Society, Stardust Hotel, Las Vegas, Nev. Mar. 28-29. Dr. Joseph R. Newton, 2000 S. 9th East, Salt Lake Ci Utah, Publicity Chairman.

Missouri State Medical Association, Sheraton-Jefferson Hotel, St. Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Lou Executive Secretary.

National Health Council, National Health Forum, Miami, Fla Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, Exec tive Director.

National Multiple Sclerosis Society, New York City, Mar. 8. M Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. 3 Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, Ne Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., Ne Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, Ma 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Execut Secretary.

Southwestern *Surgical* Congress, *Riviera Hotel,* Las Vegas, Nev., Ma 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma C Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Sem Hotel, Mobile, *Apr. 21-23.* Mr. W. A. *Dozier Jr., 19 S. Jackson* Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla., A 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Execut Secretary.

American Association of Anatomists, Statler-Hilton, New York C Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Medici Univ. of Pa., *Philadelphia 4, Secretary-Treasurer.*

American Association of Immunologists, Chicago, Apr. 11-15. I Calderon Howe, Columbia Univ. College of Physicians and Surgeo New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, Ho Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman, De of Pathology, L. S. U. School of Medicine, New Orleans, La., Secreta

American Association of Railway *Surgeons, Drake Hotel,* Chica Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chicago Executive Secretary.

American College of Obstetricians and Gynecologists, Netherla Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardson, 79 Monroe St., Chicago 3, Executive Secretary.

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American College of Surgeons, Sectional Meeting, Hotel Leamingt Minneapolis, Apr. 11-13. For information write: Dr. H. P. Saunde 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Kahler Ho Rochester, Minn., Apr. 14. For information write: Dr. H. P. Saunde 40 E. Erie St., Chicago 11.

American Dermatological Association, Inc., Boca Raton Hotel, B Raton, Fla., Apr. 8-12. Dr. Wiley M. Sams, 308 Ingraham Bldg., Mia 32, Fla., Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. Da D.Sc., 9650 Wisconsin Ave., Washington 14, D. C., Executive Secreta

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SURVIVAL OF PATIENTS WITH INJURIES OF THE SPINAL CORD

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and
Harry Kessler, M.D., Washington, D. C.

In order to compare the longevity of paraplegic or quadriplegic patients with the longevity of the general population, special statistical procedures have been developed. Data from a series of 5,575 patients grouped according to age permitted comparison with corresponding age-groups from the general population. During the first year after the trauma to the spinal cord the patients showed a mortality 5 to 10 times as high as that among patients who survived the first year. Thereafter the life expectancy increased markedly. Of a group of paraplegic or quadriplegic patients who were under 35 years of age at time of injury and who had survived the first year after injury, 80% were likely to be alive 10 years after injury. The disparity of life expectancy between injured and normal people increased markedly in the older age-groups.

OVER the past 15 years Veterans Administration hospitals, in particular the seven centers established for the care of spinal cord injuries, have provided medical care for thousands of veterans disabled by paraplegia or quadriplegia after spinal cord injury. These services have been extended both to veterans disabled by injuries or wounds received during war service and to other veterans with non-service-connected paraplegia or quadriplegia who are unable to defray the cost of hospital care required for their condition. An analysis of the survival experience, or longevity, of a large series of consecutive patients treated in Veterans Administration hospitals may be of interest to clinicians and practitioners of forensic medicine.

In September, 1955, a survey was conducted to assemble information on the demographic and clinical characteristics of the 5,743 patients who had been treated for traumatic paraplegia or quadriplegia in a Veterans Administration hospital one or more times between Jan. 1, 1946, and Sept. 30, 1955. Each reported veteran has been followed up through the Veterans Administration records system and mortality data obtained from death certificates filed in the veteran's claim folder. While notices of death have been received routinely and are current, we have limited our survival analysis to the reported experience up to Oct. 1, 1956.

From the Department of Medicine and Surgery, Veterans Administration.

Method of Study

If the patients had all been injured on the same day, say Oct. 1, 1946, and if they all had been brought immediately to a Veterans Administration hospital for treatment of their spinal cord injury and resulting paralysis, it would be a straightforward matter to describe their 10-year mortality experience to Oct. 1, 1956. The probability of death could then be computed as the ratio of the number of patients dying in the 10-year period to the number of patients injured on Oct. 1, 1946.

TABLE 1.—*Selected Patients* with Traumatic Paraplegia and Quadriplegia Treated in Veterans Administration Hospitals*

Age at Injury, Yr.	Total No.	Paraplegics, No.	Quadriplegics, No.
15-24	2,452	1,845	607
25-34	2,212	1,705	507
35-44	606	450	156
45-59	305	198	107
Total	5,575	4,198	1,377

* All patients were under observation at some time within 11 years of injury and were under 60 years of age at time of injury.

All of the 5,743 patients who were studied, however, were not injured on the same day. Moreover, most of them were not hospitalized by the Veterans Administration immediately after their injury but were admitted to the VA hospital by transfer from a military or private hospital. Thus, only a small percentage of the 5,743 patients were under observation during a period when the likelihood of death is greatest. Moreover, by October, 1956, only a small proportion of the patients had been observed continuously for 10 years from the time of injury. Hence, the simple mortality ratio would not provide a valid index of the likelihood of death, or of its complement, the probability of survival after traumatic paraplegia or quadriplegia.

The life table method provides an estimate of the survival experience by including the experience of each patient only for the period of time when he was actually under observation. For example, a patient admitted to a VA hospital on Oct. 1, 1946—two years after his wartime injury—is included in the survival calculations only for time periods after the second year. If he survived until Sept. 30, 1956, he is included for a 10-year period extending from the 3rd through the 12th year after injury. The rationale for this procedure is based on the assumption that his experience after the second year is similar to that of all other similarly disabled patients who survived to this point in time after their injuries. (A more complete description of the methodology used may be obtained from the Biometrics Service, Department of Medicine and Surgery, Veterans Administration, Washington 25, D. C.)

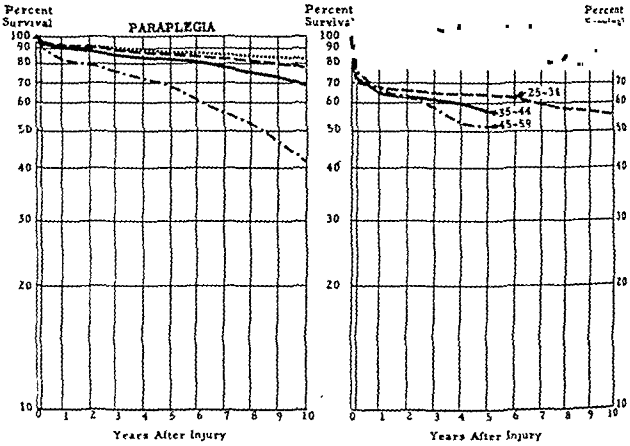
TABLE 2.—*Percentage of Patients with Traumatic Paraplegia and Quadriplegia Surviving For Specified Time Periods After Injury*

Survival Period After Injury	Paraplegics, by Age, %				Quadriplegics, by Age, %			
	15-24	25-34	35-44	45-59	15-24	25-34	35-44	45-59
1 mo.	94	95	94	91	89	70	73	76
1 yr.	92	92	92	82	87	68	64	66
5 yr.	88	86	83	69	83	64	57	51
10 yr.	81	79	69	41	77	55	*	*

* Not calculated because of small number of patients observed in age group.

Survival Data

The actuarial analysis was limited to those patients who were under 60 years of age when injured and who were under observation in Veterans Administration hospitals at some time during an 11-year-period after the onset of their paralysis. These restrictions reduced the number of patients in the group from 5,743 to 5,575.



Survival curve according to age of patient.

In table 1 the data of patients are shown distributed by age at the time of their injury and according to the nature of their paralysis. Of the total group, 84%, or 4,664 patients, were between 15 and 35 years of age when injured. Three-quarters of the group, or 4,198 patients, were treated in Veterans Administration hospitals for traumatic paraplegia, and the remaining 1,377 study patients had suffered traumatic quadriplegia. The two smallest subgroups studied were quadriplegics in the group aged 35 to 44 years (156 patients) and quadriplegics between 45 and 59 years of age (107 patients).

The survival data of each of the eight subgroups are summarized in table 2 and in figure 1, in terms of the percentage of those of each group who might be expected to be alive at specified time points after injury. These data indicate that the likelihood of survival after hospitalization for traumatic paraplegia or quadriplegia decreases with advancing age, particularly for patients who were over 45 years of age when injured. Of every group of 100 paraplegics between 15 and 25 years of age at time of injury, 81 will probably be alive 10 years later. The 10-year-survival rates decreased to 79, 69, and 41%, respectively, for patients with paraplegia in the groups aged 25 to 34, 35 to 44, and 45 to 59 years. Quadriplegic patients do not fare as well as patients of comparable age with paraplegia. While 77% of traumatic quadriplegic patients 15 to 25 years of age when injured can be expected to survive for 10 years, the 10-year-survival rate among quadriplegic patients 25 to 34 years of age is estimated to be only 55%. Estimates of time of survival were not computed for the entire 10-year period for patients with quadriplegia between 35 and 59 years of age because too few patients were observed later than the fifth year after injury to permit the computation of reliable rates. However, on the basis of the 5-year survival experience for the older quadriplegic patients studied, it can be estimated that less than half of them survive for 10 years after their injuries.

The survival curves shown in the figure graphically reflect the high mortality of patients treated for paraplegia or quadriplegia during the first month after a spinal cord injury. The prognosis during this high-risk period is much poorer for quadriplegic patients, particularly for those over 25 years of age. While the fatality rate among paraplegic patients during the first 30 days after injury is between 5 and 10% (depending on their age), it is about 30% for quadriplegic patients over 25 years of age. Between the 1st and 12th month after injury, fatality rates decrease precipitously, but they are still relatively high as compared with mortality observed after the first year.

The relative flatness and constant slope of each of the survival curves between the 1st and 10th year after injury indicates that those patients who are alive a year after injury have a relatively low and fairly constant annual mortality over the next nine years. The survival computations shown in table 3 exclude the high mortality period immediately after injury and represent the percentage of paraplegic and quadriplegic patients who are expected to survive for at least 10 additional years after the first anniversary of their injury. These data indicate that the mortality differentials between patients with paraplegia and those with quadriplegia during the first year after injury are not maintained during the subsequent 10-year period.

Table 3.—*Percentage of Recovered Traumatic Paraplegic and Quadriplegic Patients* Surviving for Specified Time Periods After Injury*

Survival Period After Injury, Yr.	Paraplegics, by Age, %				Quadriplegics, by Age, %			
	15-24	25-34	35-44	45-59	15-24	25-34	35-44	45-59
6	95	92	88	74	94	91	87	76
11	86	84	75	48	88	81	†	†

* Recovered paraplegic or quadriplegic patient is one who has lived at least one year after injury.

† Not calculated because of small number of patients observed in age group.

Table 4.—*Percentage of Recovered Paraplegic and Quadriplegic Patients* and of Male Population† of the United States Surviving For Ten Years, by Age Group*

Age Group, Yr.	Ten-Year Survivors, %			Average Annual Mortality per 100 Patients in Excess of that of U.S. Male Population	
	U.S.† Men	Recovered Paraplegics	Recovered Quadriplegics	Paraplegics	Quadriplegics
15-24	98	86	88	1.2	1.0
25-34	97	84	81	1.3	1.6
35-44	94	75	‡	1.9	‡
45-59	83	48	‡	3.5	‡

* Recovered paraplegic or quadriplegic is one who has lived at least one year after injury.

† Based on mortality rates observed in 1949-1951: survival rates in each age group adjusted to age distribution of paraplegic and quadriplegic patients within age group.

‡ Not calculated because of small number of patients observed in age group.

The patient with quadriplegia who does not die during the first year after his injury (referred to as recovered) is found to have almost as good a chance of living for 10 more years as a recovered patient with paraplegia of comparable age. Of recovered paraplegic or quadriplegic patients between 15 and 35 years of age at time of injury, more than 80% can be expected to be alive 11 years after injury.

While the survival record of recovered patients is heartening, it is, of course, not as good as that of persons of comparable age in the general population, as shown in table 4. The excess mortality among "recovered" paraplegic or quadriplegic patients over that of the general population of corresponding age increases with advancing age. The annual excess mortality is between 1 and 2 per 100 recovered patients under 25 years of age when injured. For recovered patients between 45 and 59 years of age, the excess mortality is probably between 3 and 4 per 100 patients per annum.

Comment

While many problems of therapy and total rehabilitation are still unresolved, physicians concerned with the care of patients with traumatic paraplegia and quadriplegia have had ample evidence of the increasing effectiveness of their treatment techniques.[1] It has also been generally agreed that current therapies have added years to the lives of these patients. Nonetheless, a review of the recent literature did not disclose any definitive statistics on the longevity of patients with traumatic paraplegia and quadriplegia after their injuries.

Dietrick and Russi[2] reported on a consecutive series of 41 patients with traumatic paraplegia or quadriplegia on whom autopsies were performed in the Veterans Administration Hospital, Richmond, Va., between April, 1946, and July, 1955. This group was reported to have lived, on the average, four years after traumatic injury to the spine. However, as demonstrated by Mainland[3] and Berkson,[4] a survival picture derived solely from an analysis of intervals between onset and death is generally less favorable than that obtained from a longitudinal study of the survival of an entire cohort of patients.

In contrast to the average survival period of four years calculated by Dietrick and Russi, it is estimated from our data that, on the average, more than 50% of any random group of patients with traumatic paraplegia or quadriplegia will be alive 10 years after their injuries. The likelihood of 10-year survival, however, is found to vary considerably with the patient's age and the severity of his injury. For paraplegic patients under 35 years of age, about 80% survive for 10 years; whereas, only 30 to 40% of a group of paraplegic and quadriplegic patients between 45 and 59 years of age can be expected to reach the 10th anniversary of the injury.

Of perhaps greater significance in the appraisal of time of survival is the fact that the mortality of "recovered" patients for the next 10 years is not markedly in excess of that of the general population of similar age. For recovered patients under 35 years of age, the excess mortality is only 1 to 2% annually. It is also of interest to note that, while quadriplegic patients as compared to paraplegic patients have an extremely poor prognosis of surviving the first year, those recovered quadriplegics who do survive appear to have as favorable a mortality over the next 10 years as paraplegic patients of the same age. Some clinicians, however, view this favorable survivorship picture with circumspection. They feel that the observed survival pattern may not continue, due to the cumulative effect of renal infection or other complications such as secondary amyloid disease. For this reason, we plan to reappraise the mortality of the group periodically on the basis of the continuous follow-up of all survivors.

The survival data presented here were derived from the average experience of patients treated in Veterans Administration hospitals between 1946 and 1955. Since it is believed that therapeutic methods have improved during this period, the survival rate of patients with traumatic paraplegia and quadriplegia currently admitted to Veterans Administration hospitals is expected to be even more encouraging.

Summary

A study was undertaken to describe the prognostic implications of demographic and clinical characteristics of 5,743 patients who had been treated for traumatic paraplegia or quadriplegia in a Veterans Administration hospital one or more times between Jan. 1, 1946, and Sept. 30, 1955. Mortality data were acquired on each deceased patient. Analysis of the survival data of 5,575 patients under 60 years of age at the time of their injury shows the following major findings.

The age-specific mortality among patients during the first year after spinal cord injury was 5 to 10 times higher than the average annual mortality among survivors during the subsequent 10-year period. Patients with quadriplegia have a much poorer prognosis of surviving the first year after injury than do paraplegic patients of the same age. Younger patients have an excellent chance of recovering from the immediate effects of the trauma and resulting paralysis. About 92% of hospitalized paraplegic patients under 45 years of age at the time of injury and 87% of hospitalized quadriplegic patients under 25 years of age can be expected to be alive one year after injury. More than 80% of the paraplegic or quadriplegic patients under 35 years of age at the time of injury are likely to be alive 10 years later if they survive the high mortality risks during the first year after injury.

As compared to the general population, in the United States, of caucasoid men of comparable groups aged under 45 years, paraplegic or quadriplegic patients who were alive one year after injury have an average annual excess mortality of between one and two deaths per 100 surviving patients. This differential increases to between 3 and 4% if the patients are in the group aged 45 to 59 years at time of injury.

Veterans Administration Central Office (25) (Dr. Kessler).

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NEWER ANATOMY OF LIVER—VARIANT BLOOD SUPPLY AND COLLATERAL CIRCULATION

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To facilitate and safeguard operative procedures on the liver and gallbladder, there has been a need for comprehensive knowledge of the varied patterns of extrahepatic arteries and bile ducts. Two hundred dissections of vessels that supply blood to the upper abdominal organs were done, and the vessels conformed to the textbook description in only 55% of the cadavers. Similarly, the incidence of the cystic artery originating from the celiac right hepatic artery was 63%. The reason found for this deviation was that hepatic arteries were sometimes derived from the left gastric and superior mesenteric arteries. In the past these hepatic arteries were considered to be accessory vessels, but such a terminology can no longer apply since each hepatic artery is known to function as an end artery. Not one can be sacrificed without a resulting necrosis of liver tissue, for each has a selective distribution to a definite area of the liver.

Historically considered, the modern types of operative procedures on the liver, gallbladder, and upper abdominal organs are relatively recent innovations in surgery. James Marion Sims, a graduate of Jefferson Medical College in 1828, was the first to perform a cholecystotomy, on April 18, 1878, in Paris and named the operation thus. The first removal of the gallbladder was made by Carl Johann August Langenbuch, a graduate of Kiel University, Germany. He successfully performed the operation on a man at the Lazarus Hospital, Berlin, on July 15, 1882. The first surgeon to remove a gallbladder in the Western Hemisphere was Justus Ohage. Born in Hannover, Germany, he emigrated to the United States and served in the Civil War. After his graduation from the Medical School of the University of Missouri, June 3, 1880, he studied surgery under Langenbuch and, on his return to this country, established his surgical practice in St. Paul, Minn. Dr. Ohage performed a cholecystectomy on a woman at the St. Joseph's Hospital, St. Paul, Minn., Sept. 24, 1886, the operation being the ninth that had been performed in the world at that time.

Pioneers in upper abdominal surgery were the Mayo brothers (Charles and William) of Rochester, Minn. Their father, Dr. William Worrell Mayo, often sent his two sons to St. Paul to watch Dr. Ohage operate, and it is said that these experiences were the first inducements the Mayo brothers had to become surgeons. It took the Mayo brothers 12 years to accumulate their first 500 operations on the gallbladder and ducts, but their second 500 were accomplished in 18 months. In December, 1904, Dr. Charles Mayo read before the Southern Surgical Association his and his brother's joint report of 1,000 operations for gallbladder disease, to prove to doubting physicians that the only effective means for a cure of a diseased gallbladder is its surgical removal. From January, 1907, to January, 1918, 5,655 operations for gallstones were performed at the Mayo Clinic, with a mortality of 2.4%. In a comparable contemporary large series, Hans Kehr, leading biliary surgeon in Germany, had a mortality of 2%.

That cholecystectomy is a dangerous operation was brought to the attention of surgeons, in 1923, by the British surgeon Flint, who said: "Technically, gallbladder surgery is much the most difficult of any abdominal surgery and inadequate appreciation of the abnormalities of this region does not lessen the risk."

This warning by Flint was emphasized and constantly supported by the late Lahey of the Lahey Clinic, who said: "We should publicize the fact that cholecystectomy is a dangerous operation. It is dangerous unless one realizes how important it is to control the blood supply, to demonstrate definitely the anatomic relationships, and to realize that anomalous anatomy is very common."

Comparable warnings and admonitions have been made by our contemporary leading biliary surgeons—Cattell, Ravdin, Cole, Walters, Behrend, and others. Their warnings have been made on the basis of their own experiences in repairing postoperatively to a cholecystectomy hundreds of cases of a surgically induced stricture or destruction of the bile ducts and impairment of the regional blood supply. One of Lahey's last statements (1950) was: "It is to be remembered that everytime a cholecystectomy is done, there is a real danger of injury to the bile ducts or hepatic artery, with the consequent possibility of producing in the patient concerned invalidism, shortening of life or an operative mortality."

From the Daniel Baugh Institute of Anatomy, Jefferson Medical College.

Read before the Section on Surgery, General and Abdominal, at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

Varied Blood Supply to Liver and Gallbladder

To facilitate and safeguard operative procedures on the liver and gallbladder, there was a dire need of exact and comprehensive knowledge of the ever varied patterns of the extrahepatic arteries and bile ducts, for standard textbooks on anatomy and surgery, up to a few years ago, offered little or no information in this respect. Cognizant of this great void in anatomic knowledge, I devoted over 20 years to an investigation of the varied blood supply of the upper abdominal organs, as ascertained in a statistical analysis of personally made dissections of 200 bodies. I published results and conclusions of this study in an "Atlas" (1955), a work called for by Haller, in 1756, after his pioneer attempt to explain, in a few pages of his "Icones," the variational anatomy of the celiac axis.

As far as the liver is concerned, the statistical analysis of 200 dissections showed that the conventional textbook description of the arterial blood supply to the liver, as effected through a celiac trunk having three branches (hepatic, left gastric, splenic), occurs only in about one-half of the population (55%), while that of the gallbladder (by a single cystic artery from the celiac right hepatic in the cystic triangle) occurs only in 63%. The reason for this astounding deviation from the typical textbook descriptions of the blood supply to the liver and gallbladder is the fact that hepatic arteries may be derived not only from the celiac trunk but also from the left gastric and from the superior mesenteric artery. Such aberrantly derived hepatic arteries have, heretofore, been termed accessory hepatic arteries. This terminology is erroneous and misleading, for, functionally considered, there are no accessory hepatic arteries, since each hepatic artery is an end artery with a selective distribution to a definite area of the liver and, therefore, cannot be sacrificed without resultant necrosis of liver tissue.

Of great surgical import is the anatomic observation that in 25% of 200 cases, the left gastric gave rise to a left hepatic artery. In one-half of these cases, it was an additive left hepatic, there being another from the celiac. In the other half of the cases, it was the only left hepatic artery present. An inadvertant severance of such a replaced left hepatic from the left gastric artery during a gastric resection would cause an ischemic necrosis of the left lobe of the liver, with resultant death of the patient (Hofmeister [7th day], Wilmer [16th day]). In 17% of 200 cases, there was an *additional right* hepatic from the superior mesenteric artery, 12% of the cases being instances in which the entire blood supply to the right lobe of the liver came from this source. Severance of such a hepatomesenteric artery, likewise, would cause an ischemic necrosis of the right lobe of the liver with fatal results (Ritter, Hofmeister).

Typically, the celiac common hepatic artery supplies three branches to the liver—right, *middle, and left hepatic. The middle hepatic artery is not mentioned in textbooks of anatomy or surgery, yet it is always present. Haller, in 1756, termed it a* hepatica media, as did Tiedemann in his "Tabulae Arteriarum" (1822). The middle hepatic courses in the umbilical fossa to supply the quadrate lobe (medial segment of the liver) and, in about equal proportion, is a branch of either the right or left hepatic artery. In some instances, it gives origin to the cystic artery, as does the left hepatic.

The amazing frequency (45%) of deviation from the so-called normal textbook type of blood supply to the liver via a celiac artery having three branches (hepatic, left gastric, splenic) is due to the fact that, in the deviating variational cases, the celiac artery is incomplete. In short, when the right or left hepatic does not arise from the celiac artery the latter becomes incomplete, and the missing right or left hepatic artery is replaced from another source, the right hepatic prevailingly from the superior mesenteric and the left hepatic from the left gastric artery. Such replacing hepatics are not to be confused with accessory hepatic arteries which are additive to the normally present right and left hepatic derived from the celiac artery. As previously stated, every hepatic artery, whether replaced from some other source, or accessory to the right and left hepatic stemming from the celiac, is functionally essential, for every hepatic artery has its specific terrain of blood supply. As is clearly demonstrable in the 100 plastic casts of livers made by Healey and Schroy in the Daniel Baugh Institute, hepatic arteries are end arteries with no anastomosis inside the liver.

Sometimes the celiac artery does not give off the hepatic artery at all, the entire blood supply to the liver then being furnished by a hepatic trunk derived from the superior mesenteric artery. Such a hepatomesenteric trunk may pass through the head of the pancreas, as may, likewise, a replaced right hepatic stemming from the superior mesenteric artery. These are constitutional, variational facts to be remembered in every resection of the head of the pancreas, lest the liver be deprived of its life-sustaining blood supply. In one case of 500 dissections, the entire blood supply to the liver, i. e., the entire hepatic trunk, came from the left gastric artery. The frequency (25%) of an origin of a left hepatic from the left gastric artery should always be borne in mind, and a detailed inspection of this common anatomy should be made in every gastric resection.

Despite the complexity, varied character, and origin of the hepatic arterial blood supply, any sample of it can, as shown in figures 1 and 2, with minor modifications, be categorized into one of the following 10 basic types supplied by the celiac hepatic artery: (1) the right, left, and middle hepatic artery (textbook type and present only in about one-half, 55%, of the subjects) (fig. 1*A*); (2) the right and middle hepatic–the left hepatic replaced from left gastric artery (10%) (fig. 1*B*); (3) the left hepatic and middle hepatic–the right hepatic replaced from superior mesenteric artery (11%) (fig. 1*C*); (4) only the middle hepatic–the hepatic replaced from superior mesenteric, left hepatic replaced from the left gastric artery (1%); (5) the right, middle, and left hepatic–the left hepatic small, hence an accessory left hepatic from the left gastric artery (fig. 1*D*); (6) the right, middle, and left hepatic–the right hepatic small, hence an accessory right hepatic from the superior mesenteric artery, (7%) (fig. 2*A*); (7) the right, left, and middle hepatic–small or of usual size–with an accessory right hepatic from the superior mesenteric and an accessory left hepatic from the left gastric artery (1%) (fig. 2*B*); (8) combination patterns of a replaced right hepatic and an accessory left hepatic or, the reverse of this, an accessory right hepatic with a replaced left hepatic artery (2%); (9) celiac hepatic absent–the entire hepatic trunk derived from the superior mesenteric artery (five cases) (fig. 2*C*); and (10) celiac hepatic absent–the entire hepatic trunk derived from the left gastric artery (one case) (fig. 2*D*).

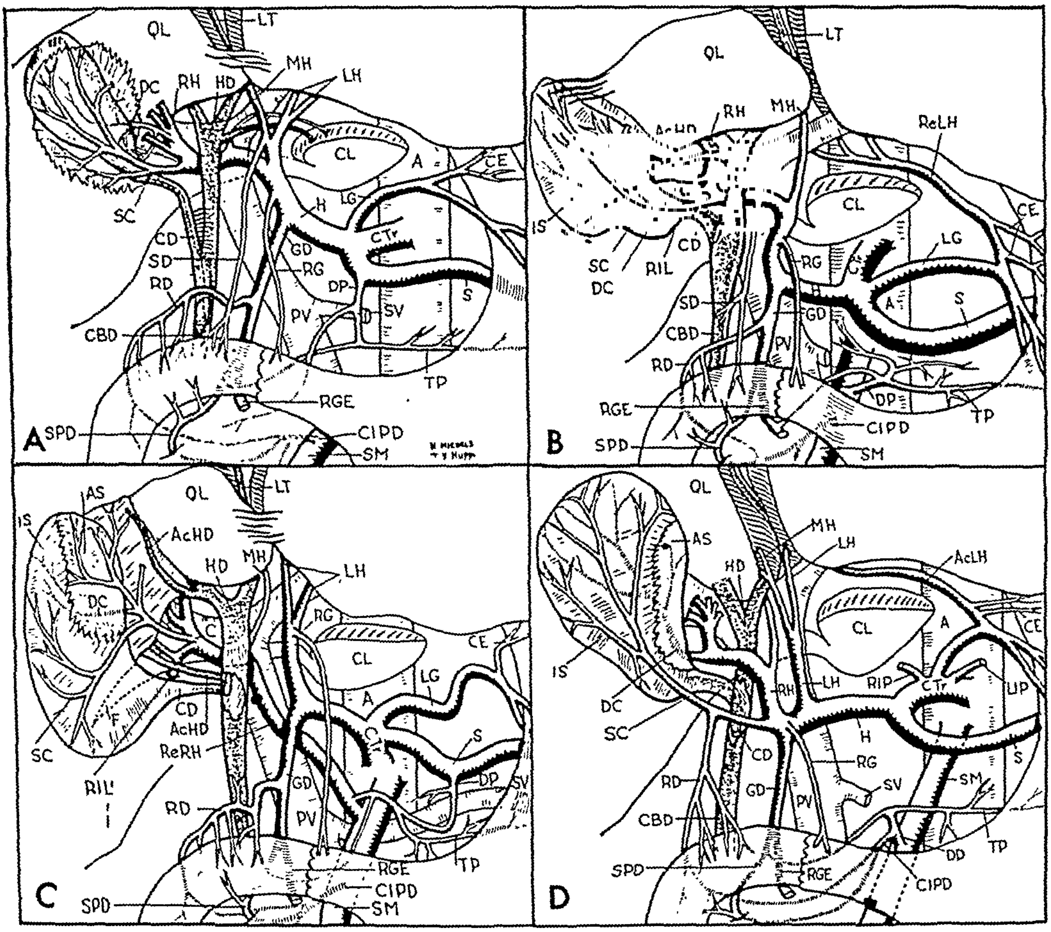

Fig. 1.—Types of hepatic arterial blood supply: *A*, right, left, and middle hepatic (55%); *B*, replaced left hepatic (10%); *C*, replaced right hepatic (11%); *D*, accessory left hepatic (8%).

Cystic Artery

Typically, the cystic artery is single (75% of cases) and arises from the celiac right hepatic artery to the right of the hepatic duct in the cystic triangle of Calot. The boundaries of this triangle are: inferolaterally, the cystic duct; medially, the hepatic duct; and cephalad, the liver. If not present, the triangle can readily be made by dissection to effect correct orientation of structures. Generally, the right hepatic and the cystic artery are in the upper part of the cystic triangle but may be anywhere within its confines. Since extrahepatic branching of the right hepatic may take place anywhere in the triangle, frequently into its two main intrahepatic segmental trunks (anterior and posterior), it follows that not every artery running parallel with the cystic duct or near it is actually the cystic artery. The supposed cystic might be the right hepatic artery, especially as, in many instances, this artery makes a tortuous, caterpillar-like loop, convexity of which abuts or strides the cystic duct or hepatic duct.

The course of the cystic artery in the triangle may be short or long, depending on its site and mode of origin. On reaching the gallbladder, it usually divides into its characteristic superficial and deep branch, these being the "cysticae gemellae" of Vesalius (1564). The superficial branch is distributed to the free peritoneal surface of the gallbladder and the deep courses behind the gallbladder, i. e., in the gallbladder bed. Both branches give off a variable number of liver twigs. Those from the deep branch, at times, are of such large caliber as to be liver vessels, inadequate attention to which in cholecystectomy may cause hidden, disconcerting bleeding.

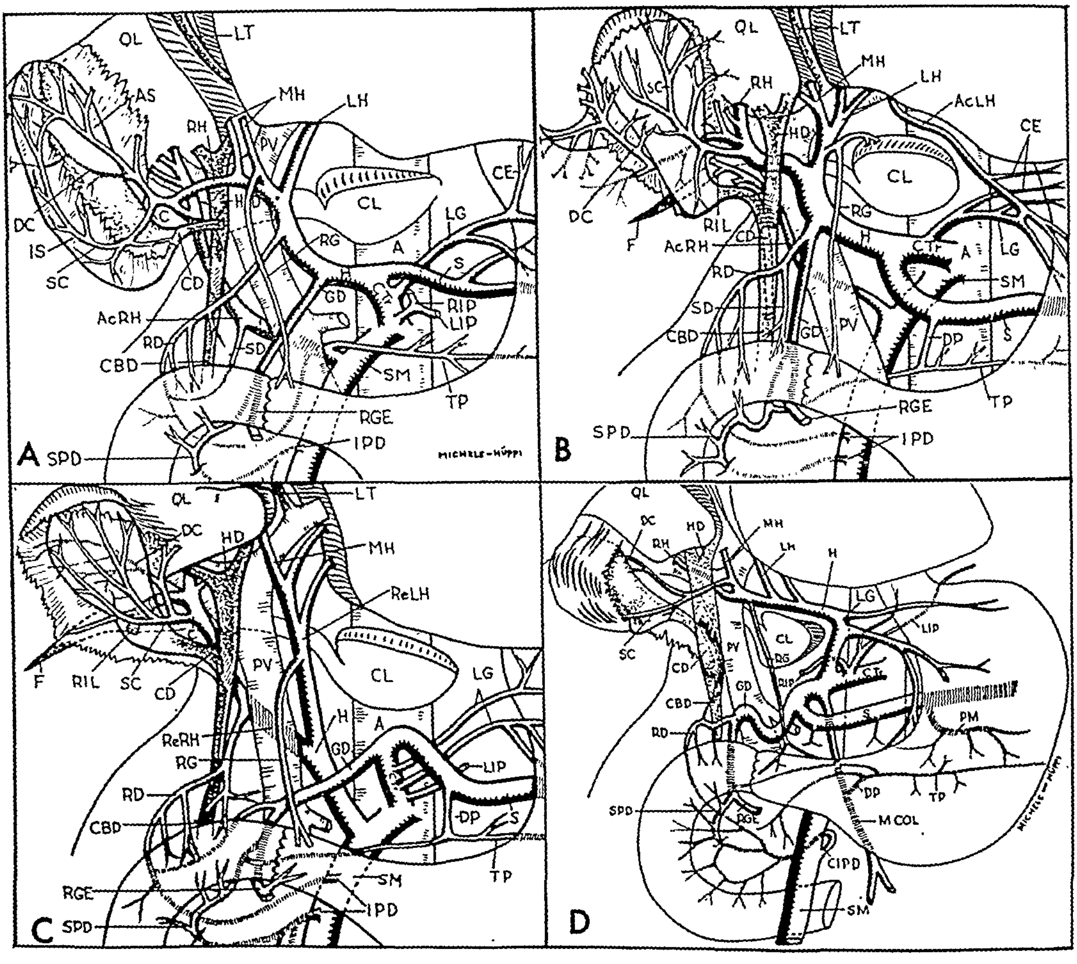

Fig. 2.—Types of hepatic arterial blood supply: *A*, accessory right hepatic (7%); *B*, accessory right hepatic and accessory left hepatic (1%); *C*, common hepatic from superior mesenteric (five cases); *D*, common hepatic from left gastric (one case).

Dual Cystic Arteries.—Dual cystic arteries are of frequent occurrence, having been observed in 25% of 200 dissections. They represent instances in which the superficial and deep branch of the cystic artery had a separate origin, either from the same right hepatic or from two right hepatics in the triangle, or one from a right, middle, or left hepatic artery and the other from some other source.

In 20% of 200 dissections site of origin of the cystic artery was not in the cystic triangle at all but outside of it, the vessel stemming from the right hepatic artery to the left of the hepatic duct (13%), from the common hepatic trunk (two cases), from the middle or left hepatic artery (5%), or from the gastroduodenal artery and its retroduodenal branch (4%). Replaced right hepatics derived from the superior mesenteric frequently (11%) give rise to a cystic artery. A common pattern of dual cystics is the one in which the superficial cystic is derived from the gastroduodenal artery, and the deep from the right hepatic in the cystic triangle. In another frequent pattern, while the deep cystic artery arises in the triangle, the superficial arises outside it from the middle or left hepatic artery. The entire blood supply to the gallbladder may come from a cystic derived from the gastroduodenal artery (two cases). In such instances, the cystic courses caudal to the cystic duct, a fact to be remembered in cholecystectomies when the cystic artery cannot readily be found in the triangle of Calot. An anterior crossing of the hepatic duct by a cystic artery (single or one of the dual variety) occurred in 25%. In eight cases, a cystic artery crossed the common bile duct; in two cases it was the entire cystic, and in six cases, the superficial branch.

Collateral Circulation of the Liver

Up to a few years ago, in both domestic and foreign textbooks of anatomy and surgery, no mention was made of the collateral, arterial pathways to the liver. Several of the newer textbooks are now listing the 26 possible collateral pathways outlined by me on the basis of my dissections of 200 bodies. Succinctly summarized, these comprise the following routes, as shown in figure 3: (1) ten basic routes (fig. 3*A*) via aberrant hepatic arteries (replaced or accessory) arising from the superior mesenteric artery, the left gastric artery, or other sources; (2) six nonhepatic routes (fig. 3*B*) capable of connecting with severed hepatic arteries: (*a*) infragastric (right and left gastroepiploic); (*b*) supragastric (right and left gastric); (*c*) infracolic (large epiploic arcade of Barkow in the posterior layer of the great omentum below the transverse colon); (*d*) paraesophageal or hepatogastric (cardioesophageal branches from left gastric and splenic uniting with similar branches of severed left hepatic artery); (*e*) retroesophageal (recurrent branch of the left inferior phrenic via union of its cardioesophageal branches with the severed left hepatic artery; and (*f*) transpancreatic (pancreatic arteries uniting with the gastroduodenal); (2) ten routes (fig. 3*C*) over arteries outside the celiac blood supply: (*a*) superior mensenteric via the inferior pancreaticoduodenal; (*b*) superior mesenteric via the transverse pancreatic; (*c*) inferior phrenic communicating with branches of the hepatic in the diaphragm; (*d*) superior phrenic from the internal mammary to the hepatic branches in the diaphragm; (*e*) falciform ligament and ligamentum teres via the "ramulus ad appendicem ensiformen" of the internal mammary (Haller) uniting with branches of the middle or left hepatic artery; (*f*) arteries coursing in the coronary, right and left triangular ligaments; (*g*) intercostals; (*h*) arteries of the posterior abdominal wall; (*i*) fine arterioles (vasa vasorum) in the hepatic veins, portal vein, and inferior vena cava; and (*j*) filamentous arterioles coursing along the biliary ducts.

It should be noted, however, that the blood supply of the liver is always unpredictable and that, because of existent anatomic variations, relatively few of the listed collateral pathways can definitely be relied on to establish an adequate, compensatory circulation in the liver when the main common hepatic trunk or celiac has been ligated. The fact that some patients have survived therapeutic ligation of the common hepatic trunk in operative procedure for portal hypertension is counterbalanced by cases in which the result was fatal.

The collateral pathways outlined here on an anatomic basis, many of them small and insignificant, should by no manner of deductive reasoning give rise to the impression that ligation of a major hepatic artery can be performed with impunity. Behrend, Gordon-Taylor, Vaughn, Gray, and Ramström definitely have committed themselves to the opinion that some of the so-called "liver deaths" after cholecystectomy are attributable to severance, ligation, or clamping of the right hepatic artery. The actual efficiency of the 26 collateral pathways to the liver that have been outlined can only be determined in further studies, such as animal experimentation, arteriograms, and postmortem investigations.

The Newer Anatomy of the Liver

A decade ago liver surgery was unknown. It was seldom attempted because of the danger of fatal hemorrhage or the fear of producing biliary fistulas by cutting of unknown intrahepatic arteries, veins, and bile ducts. With the development of modern surgical technique, partial removal of liver tissue and resection of one-half or of an entire lobe of the liver are being successfully performed daily, with increasing frequency, for the removal of benign tumors and cancerous growths. Hundreds of patients with lung cancer are now being saved by surgical removal of a cancerous lobe or segment thereof, this being possible by the recently made anatomic discovery that the lung is a segmental organ (Huber and Jackson). That the liver is, likewise, a segmental organ, with definitely delimited vascular and biliary cleavage planes, is now a well-established and at present universally accepted anatomic basis for liver resections.

The old concept that the liver is divided into a right and left lobe by the falciform ligament, the left sagittal fossa, and the ligamentum venosum is erroneous and should be abandoned in textbooks of anatomy and surgery. The correct morphologic division between the right and left lobes is made by the "lobar fissure" which, on the visceral surface of the liver, corresponds to a line extending from the gallbladder inferiorly to the fossa for the inferior vena cava superiorly. A division of this type of bilaterality was first described by Cantlie (1898) and substantiated by McIndoe and Counsellor (1927). Hjortsjö, of Sweden (1952), was the first to report, on the basis of observations

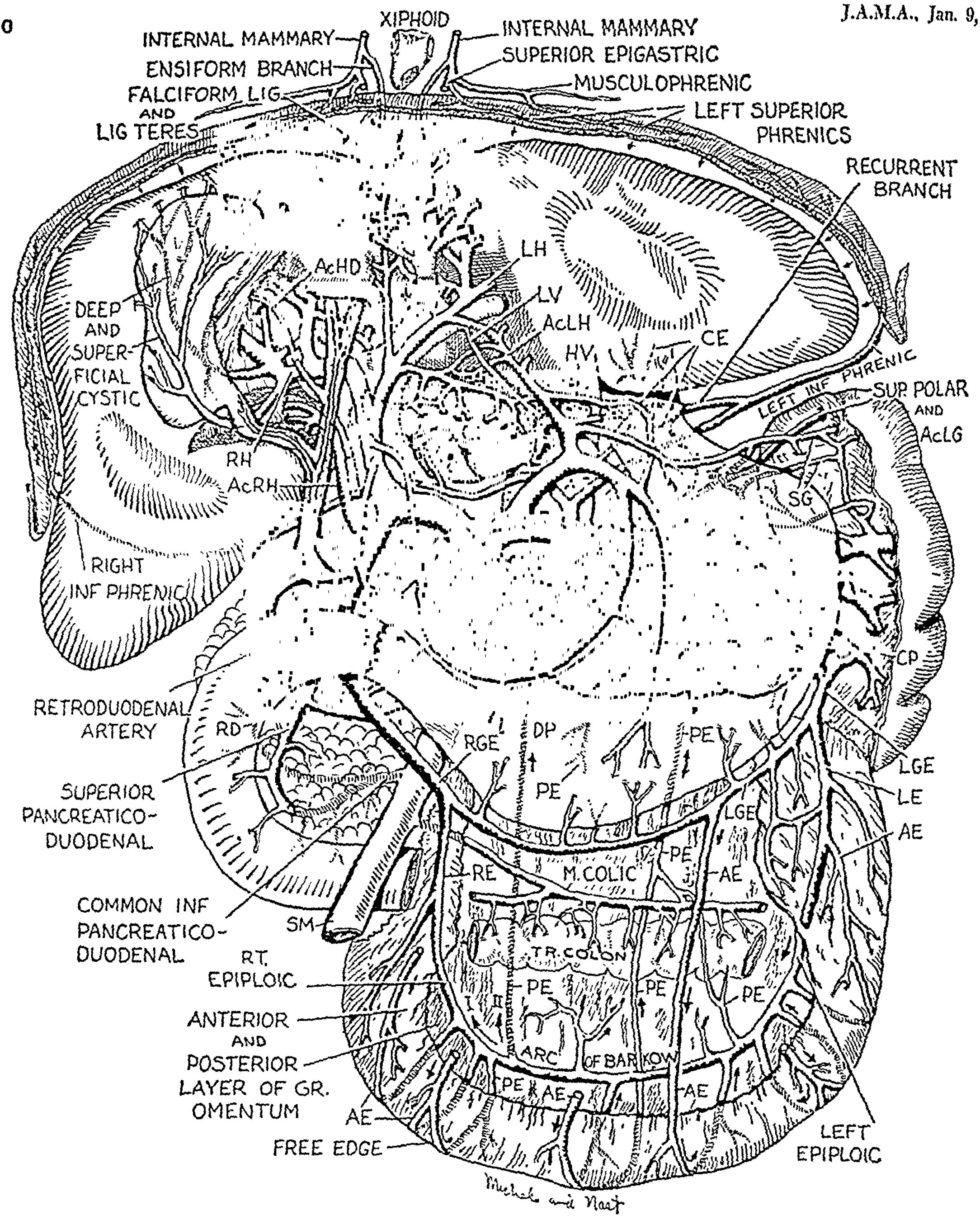

Fig. 3.—Some of the 26 collateral arterial pathways to the liver, as ascertained in 200 dissections: *A*, Routes through hepatic arteries *arising from sources other than the common celiac hepatic trunk.* 1. Accessory left hepatic (*AcLH*) from the left gastric (*LG*). 2. *Accessory right hepatic* (*AcRH*), from superior mesentric (*SM*). *B*, Nonhepatic routes capable of connecting with branches of severed hepatic arteries: 1. Infragastric *via right and left* gastroepiploics (*RGE*> <*LGE*) and gastroduodenal (*GD*) to the right, and short gastrics (*SG*) to the left. 2. Supragastric, via right and left gastrics (*RG*> <*LG*). 3. Infracolic, via the arc of Barkow *in posterior layer of the great omentum,* blood may be routed directly into the gastroduodenal (*GD*) through right gastroepiploic (*RGE*) and right epiploic (*RE*) in Type 1; indirectly into it via posterior epiploic (*PE*), transverse pancreatic (*TP*) and its connections in Type 2. *Left limb of arc is always made by the left epiploic* (*LE*). 4. Paraesophageal—or hepatogastric. Cardioesophageal (*CE*) branches from the left gastric (*LG*) and *splenic* (*S*) via its short gastrics (*SG*) unite with similar branches from accessory left hepatic (*AcLH*). 5. Retroesophageal. Recurrent branch of left inferior phrenic gives off cardioesophageal (*CE*) branches that unite with those derived from accessory left hepatic (*AcLH*), short gastrics (*SG*), and accessory left gastric (*AcLG*). 6. Transpancreatic. Blood leaving the splenic (*S*) through the dorsal pancreatic (*DP*) or a. pancreatica magna (*PM*) and caudal pancreatic (*CP*), or coming from the arc of Barkow through a posterior epiploic (*PE*) enters the transverse pancreatic (*TP*) *via* which it may course into the superior pancreaticoduodenal (*SPD*), right gastroepiploic (*RGE*) or gastroduodenal (*GD*) to reach the hepatic trunk (*H*). *C*, Routes over arteries outside the celiac blood supply. 1. Superior mesenteric (*SM*) via the inferior pancreaticoduodenal and the anterior and posterior pancreaticoduodenal arcades, respectively, made by the retroduodenal (*RD*) and superior pancreaticoduodenal (*SPD*), branches of the gastroduodenal (*GD*). 2. *Superior* mesenteric via its transverse pancreatic (*TP*) branch, which may connect with the *SPD*, *RGE* or *GD*. 3. *Inferior* phrenics coursing in the diaphragm unite with branches of the hepatic at attached areas of liver. Cardioesophageal (*CE*) branches of the recurrent branch of the left inferior phrenic anastomose with subcapsular branches of the hepatic in *fossa for* ligamentum venosum. 4. *Superior* phrenic from the terminal branches of the internal mammary, i.e., superior epigastric and musculophrenic communicate with branches of hepatic in diaphragm. 5. Ensiform branch of the internal mammary (Haller, 1756) coursing in the falciform ligament and ligamentum teres unite with terminal falciform branches given off by the left (*LH*) and middle hepatic (*MH*). 6. Vasa vasorum. An arteriole derived from the right *inferior* phrenic courses upward to liver along inferior vena cava (*IVC*). 7. Supply along the biliary ducts by arteriole derived from the retroduodenal (*RD*).

made on 12 injected corrosion casts, that the liver is a segmental organ, the hepatic arteries, bile ducts, and portal vein branches having a definitive segmental distribution inside the liver. Elias and Petty (1952) substantiated this finding in five corrosion casts of human livers made with a plastic material.

Without any knowledge of Hjortsjö's work, Healey and Schroy, at the Daniel Baugh Institute, had been investigating the intrahepatic distribution of the Glissonian triad (arteries, portal vein, and bile ducts) in a large series of vinyl acetate–corrosion casts and had come to the same conclusion as Hjortsjö, to wit, that the liver was divided by fissures into definite segments. When learning of Hjortsjö's work (1951), Healey and Schroy continued their investigations on an extended scale and made a statistical analysis of the intrahepatic distribution of bile ducts and hepatic arteries, as observed in 100 vinyl acetate-corrosion casts. This first statistical report, published in 1953, definitely proved that the liver is a segmental organ, with variant patterns of the segmental distribution of bile ducts and arteries.

The plastic casts show that a main lobar fissure divides the liver into a right and left lobe. No indication of the presence of this fissure can be seen on the parietal surface. It is readily observable only in casts in which the hepatic veins have not been injected, for one of the main trunks of the hepatic veins (the middle one) runs in this fissure within the liver substance. In contrast with the hepatic veins, no branches of the bile ducts, the hepatic arteries, or the portal vein ever cross the main lobar fissure in these casts, proving thereby that, surgically considered, there are safe sites for liver incisions and resections.

As can be readily observed in casts, each lobe (right and left) is further subdivided into two segments by a fissure. A right segmental fissure, best seen when viewing the casts from the right side, divides the right lobe into an anterior and posterior segment. A left segmental fissure divides the left lobe into a medial and lateral segment. In position, this left fissure corresponds to the surface marking customarily used to divide the liver into a right and left lobe, i. e., on the parietal surface to the attachment of the falciform ligament and on the visceral surface to a line running through the umbilical fossa below and through the fossa for the ligamentum venosum above.

The lateral segment of the left lobe corresponds to the left lobe of the liver, as described in textbooks. The medial segment corresponds, on the visceral surface, to what textbooks designate as the quadrate lobe and on the parietal surface to all the area between the main lobar fissure and the left segmental fissure.

On the basis of its arterial blood supply and biliary drainage, therefore, the liver comprises four segments, to wit: an anterior and a posterior segment for the right lobe and a medial and lateral segment for the left lobe. Each of the four segments is subdivided into a superior and inferior area, with one specific superior and inferior area bile duct and artery, except for the medial segment where the superior and inferior area bile ducts and arteries are double.

The caudate lobe, according to its biliary drainage and blood supply, may be divided into three parts: the caudate process and the right and left part of the caudate lobe proper. Prevailingly, three bile ducts drain and two arteries supply the caudate lobe, there being one bile duct for each of its parts, one artery for the caudate process and the right half of the caudate lobe proper, and one artery for the latter's left portion.

Comment

A knowledge of the intrahepatic anatomy of the bile ducts and the blood vessels is of paramount importance to the surgeon and to the roentgenologist. In the performance of a complete right or left hepatic lobectomy and in partial hepatectomies for removal of solitary benign or malignant neoplasms, a knowledge of the normal anatomic pattern is indispensable in order that correct, fairly bloodless incisions be made and life-sustaining arteries preserved. Cholangiography as a roentgenologic method for exploring bile ducts at operation is being utilized with increasing frequency and good results. With further improvements, cholangiography may become very useful in the diagnosis of various liver diseases, such as congenital anomalies of the bile ducts, fibrotic conditions of the liver that cause the bile ducts to become narrow and tortuous, or tumor formations that cause a displacement of the bile ducts.

From this extensive anatomic study, the conclusion is warranted that every major artery of the liver (normal, replaced, or accessory) supplies a definite segment of hepatic parenchyma and that every bile duct, including the so-called accessory hepatic ducts, (17% in 200 dissections) drains a definite segmental area of the liver.

Arterial variations, like other anatomic variations, cannot be ignored, for the risks of ligating the wrong vessel or of severing an essential organ-sustaining artery, together with the dangers of ischemia and gangrene and of leakage and bleeding from sites of repair and at anastomotic suture lines are too great and constitute ubiquitous possibilities. Arterial variations are verifiable facts of the human constitution that have been observed time and time again. They can be statistically estimated by dissection of a large series of bodies and should, accordingly, be summed up in the lowest common denominators readily available to the anatomist for teaching and to the surgeon as a guide and precaution in operative procedures. William Stewart Halsted, who introduced the use of rubber gloves in surgery in 1891, spent years of his life in a serious and vigorous campaign to educate prospective surgeons to keep abreast with anatomy and, in particular, to have a healthy respect for life-sustaining arteries when operating. He stated truly and effectively, (1921): "The surgeon's method of dealing with the blood vessels is a criterion of his proficience in his art."

307 S. 11th St.

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PROGRESSIVE PATIENT CARE

A PRELIMINARY REPORT

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Increasingly frequent complaints in a 187-bed community hospital led to drastic reorganization of services on the basis of the amount of nursing care needed by the individual patients. Three units were developed at first: (1) special care unit for the seriously ill, (2) intermediate care unit, and (3) self-service unit for those able to answer their own bodily needs. Later a (4) continuation care unit, restoration-oriented, was developed for patients with such conditions as hemiplegia and cancer. In order to effect such changes it is necessary to involve the hospital trustees, administration, nurses, and medical staff from the beginning. The plan is referred to as progressive patient care. It must be kept flexible. Systematic comparisons with 17 other hospitals showed that it has substantial advantages as to the number of employees needed per hospital bed, the total patient cost per day, and the wages and salaries that can be paid to hospital personnel.

A 39-year-old hospital in New England was studied because of "growing pains." The symptoms were represented by rising costs, nursing problems, administrative difficulties, and unhappy patients. First evident in World War II and constant since that time, they were manifested by derogatory letters to the administrator about problems ranging from a glass of water to a back rub and a pair of false teeth. Griping pains and borborygmi occurred in the doctors' lounge concerning patient care, handling of emergency admissions, "week-enditis," and inability to obtain adequate private duty nurses. General cephalgia arose among the nursing staff at their inability to be all things to all people. A persistent hyperreflexia was apparent in the board of trustees regarding increased hospital costs. But most obvious was an apparent malaise of all concerned when considering ways to adequately meet the problems.

History

The development and history of the hospital were of importance. The hospital was the only one in the community of Manchester, Conn. The town had a population of about 40,000 and was situated only 11 miles from Hartford, where several large hospitals had their diversified units of specialization. Since it was located midway between New York and Boston the medical family background was divided between the various medical schools, with a strong family influence from nearby Yale. The population had grown from 20,000 persons in 1920 to 70,000 persons served by the hospital in 1959. The initial 50-bed hospital had expanded through four building programs in 1925, 1941, 1952, and again in 1959 to a present capacity of about 300 beds. The original staff of 14 physicians had mush-

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From the Manchester Memorial Hospital.

roomed to the present active staff of 61 physicians, with most of the specialties except neurosurgery and cardiac surgery represented.

A complete physical examination of the hospital revealed an adequate physical plant with community growth generally ahead of hospital expansion. At the time of the study the hospital contained 187 beds with about 135 beds devoted to adult medical and surgical patients. The building appeared well maintained and adequately decorated. The equipment was suitable and reasonably up to date.

In summary, the chief complaint obviously represented a functional disease. Active treatment began in 1956 with the appearance of a new hospital administrator who spearheaded the formulation of his ideas about reorganizing patient care into the broad program we now know as progressive patient care.

Progress Report

The idea of progressive patient care, as originally discussed informally with several members of the medical staff, resulted ultimately in the formation of a long-range planning committee. This committee was comprised of ourselves with Mr. Elmer Weden, the president of the board of trustees. Only after many evening hours spent in friendly and sometimes vociferous debate did the program begin to take shape.

Philosophically, the program is patient-oriented. The patient is the *raison d'être* of the hospital, therefore his total needs are considered. The doctor-patient relationship is the hub of patient care. All other services such as dietary, nursing, physiotherapy, and diagnostic procedures radiate from this center of activity as the spokes of a wheel. Forming the rim and holding each in its proper perspective and function is the administrator.

Disease, per se, has many phases. In recent years, it has been the habit of physicians to classify, sort, and catalog illnesses in order to seek specific entities and effect specific cures. However, a study of acute disease from a different viewpoint reveals that patients do have something in common—a degree of illness. There are three groups of patients, according to phase of disease: (1) the seriously ill, who may be unable to make their needs known, or who demand a large amount of nursing care; (2) those ill, but not seriously so, who are able to make their wishes known; and, finally, (3) those who are able to answer their own bodily needs but still require hospital services.

Evidence in support of the theory of progressive patient care is developing.[1] In research on nursing services, under the direction of Dr. Charles D. Flagle at the Johns Hopkins Hospital, a work measurement study has shown the existence of the following three levels of need, depending on patients' degree of self-sufficiency: (1) intensive-care patients receiving an average of two and one-half hours of direct care; (2) intermediate-care patients receiving an average of one hour of direct care; or (3) self-care patients receiving about one-half hour of direct care.

Progressive patient care consists of the systematic classification of patients according to their medical needs. Instead of organizing the hospital from either the economic status or type of disease viewpoint (i. e., medical-surgical service) as had been done previously, it was planned according to the phase of the patient's disease. Since there are in acute disease three types of patients, three units were developed as follows: (1) special care unit—for the seriously ill; (2) intermediate care unit—for those ill, but not seriously so; and (3) self-service unit—for those able to answer their own bodily needs.

To facilitate this change, a committee was formed of the various members of the hospital family. It was later found expedient to develop a committee for each unit of care. Each committee was headed by a physician and composed of other doctors, the administrator, nurses, trustees, dietitians, housekeepers—and any other person involved in the problems being studied. The committees evaluated the problems of patient care for their respective unit, developed policy, regulated and corrected errors as they arose, and planned future development. Problems of patient care were documented and reported at the various committee meetings by a physician or nurse. Since all members of the hospital organization were represented, definite answers to problems were logically developed. While at first monthly meetings were necessary, more recently the various committees have met only two or three times a year.

Development of Program

The special care committee was formulated first. Initially it catalogued patients to determine the number of special care unit patients present in the hospital at any given time. An appropriate area was then selected and developed as a special care unit. Visits were made to other hospitals to study existing units and facilities. Staffing patterns were developed by the nursing department. Equipment and medicaments that would be necessary were tabulated by the physicians. Special nursing procedures and techniques were considered and a nursing routine established. Special charts were developed.

Plans were developed in a similar manner for the other units. After the plans had been completed for each unit the total program was submitted to the medical staff for approval. Considerable interest and stormy debate resulted. After a lengthy evening meeting the over-all program was accepted. It required two meetings of the board of trustees to obtain their acceptance of the novel program. With medical staff participation assured the program began—and the three units, special care, intermediate care, and self-service care, started to function simultaneously.

That chronic disease was a problem in the hospital became apparent from operational experience. Unexpected help came from an illuminating study of five acute general hospitals in Boston by Rosenfeld and associates.[2] He had found that 2 to 9% of patients in an acute general hospital really suffer from chronic illness and require a large amount of nursing time. With this study in mind a chronic care committee was formed and a continuation care unit eventually was placed in operation to concentrate these patients in one area.

Chronic disease patients appeared in the hospital for two reasons—either by exacerbation of their chronic disease or from a complicating illness in addition to their primary disease. The problems of chronic disease are handled by the nursing staff with the guiding philosophy aimed at restoration of function to the level of activity of daily living.

The original program was instituted on April 1, 1957, at minimal cost and with little change in the physical plant. The special care unit expenses were less than $1,000. Renovation and repairs, including the installation of several lavatories and an automatic sprinkler system in the self-service unit known as Crowell House cost approximately $13,000. It was the functional organization, however, that was important. An adequate physical reorganization of the hospital was not possible, particularly in the self-service area. Many more beds of this type could have been utilized. The lack of adequate numbers of self-service beds is important in a total evaluation of the program. However, despite obvious inadequacies, results have been most encouraging. And now, in order to present the results in a logical manner, the findings are discussed in relation to the various units.

Special Care Unit.—On the special care unit during more than two years of operation it was possible to admit all emergency patients without delay, bypassing the admitting office; all valid emergencies received immediate care. Reorganization of the unit eliminated the former mad rush for equipment, drugs, and supplies. Through experience, the physicians and nurses were able to locate essential emergency supplies and equipment directly in the unit.[3]

Surgical cases constituted about 60% of the case load. They included patients with intestinal perforation, gastrectomy, cholecystectomy, hysterectomy, pneumonectomy, prostatectomy, eye operations, infected or traumatic surgical wounds, and surgical problems complicated by other diseases. Medical cases constituted the remainder of the case load. They included patients with acute myocardial infarction, massive overwhelming infection, pulmonary embolism, gastrointestinal bleeding, intracranial hemorrhage, neuropsychiatric problems including attempted suicide, delirium tremens, or other acute mental disturbances. A small number of acute pediatric cases were handled. They included croup, aspirated foreign body, addisonian crisis, and splenectomy for bleeding due to trauma or hemorrhagic diathesis.

With such diversification of problems, three types of special care facilities were essential: (1) an open area for observation of several patients at one time; (2) private accommodations to control the environment from the standpoint of isolation, noise, restraint, or rest; (3) a flexible zone of semiprivate beds to maintain continuity of care in the unit.

Men and women have shared the open area when necessary. Patient resistance to this has been minimal, but some families objected. When the physician took time to explain the unit and its function to the family this problem was alleviated. Facilities were provided for the family in a small waiting-room in the unit. Constant presence at the bedside was discouraged by the simple expedient of removing all furniture from the patient's room.

One of the additional benefits of the special care unit consisted of taking over the function of the recovery room after 4 p. m. when the recovery room was closed. A valid record of vital signs and fluid balance of each patient was available through the continued presence of a highly trained group of nurses who observed the patients constantly on a fixed routine. All the nurses on this unit were trained to administer fluids intravenously. Since 90% of intravenous therapy in the hospital was performed in this area the need for a team to administer such treatment no longer existed. The flexible zone of the special care unit allowed a rapid shift of patients or nursing staff to provide a changing pattern of care for emergencies as they arose without disrupting the level of care in other areas of the hospital.

Intermediate Care Unit.—The intermediate care unit provided an average degree of nursing care. The severely ill patient was segregated in the special care unit. The alert ambulatory patient, who formerly demanded and received a large amount of nursing care, although he was capable of answering his own demands, was transferred to the self-care unit. The level of nursing care on the intermediate care unit then became relatively stable, with a persistent high level of occupancy. The unit in essence was comparable to the routine nursing area of the acute general hospital.

Patients on this unit included persons with uncomplicated appendectomies, hemorrhoidectomies, varicose vein ligations, and medical problems such as pneumonia, colitis, and hepatitis. This unit comprised the greatest percentage of hospital beds. The majority of patients have been admitted to, remained on, and gone home from this unit. Their medical needs remained constant throughout their hospital stay.

Self-Care Unit.—The self-service care unit handled three types of inpatient ambulatory problems: therapeutic, postsurgical convalescent, and diagnostic. They represented a sizable proportion of the acute general hospital population. From a therapeutic standpoint the unit proved to be a useful new tool for the medical man, allowing him to study and train his diabetic patients in self-care and diet maintenance. The postcoronary patient regained confidence and went home, certain of his ability to carry on in the community. The mild depressive was handled well on this unit. From the convalescent standpoint the surgeons found the unit useful for the last few days of hospitalization to prepare the patient for his return home after major surgery. In short, it was a whole new therapeutic tool which allowed the physician to study the patient in an environment more like that of average daily living. The alert recuperating patient no longer had his rest disturbed by an acutely ill roommate.

Continuation Care Unit.—The continuation care unit assumed the problems of care in hemiplegia, amputation, severe trauma, malignancy, and severe intractable cardiac decompensation. The unit did not involve the complicated procedures of rehabilitation but was restoration-oriented. The nurses provided care centered about a program directed at the activities of daily living.

Benefits of Program

Unfortunately, it is not possible in this paper to present individual cases—but a brief review of some of the ancillary benefits of the program are in order. The art of medicine is not an exact science. One of the main charges leveled at modern medicine is that we treat the disease instead of the patient. We are too scientific. Progressive patient care has once again allowed us to go back to the patient as an entity and treat each person according to his medical needs. Flexibility, both as to method and as to degree of care, is possible and beneficial to both patient and physician. The patient is allowed to retain his individual dignity. The vast majority of patients enter, remain, and go home from the initial unit of admission. Other patients, however, do move from one unit to another as the physician deems necessary.

The surgical patient admitted to the self-service unit had his diagnostic studies performed there, moved to the special care unit the night before surgery and received his preoperative anesthesia, went to surgery, recovery room, back to the special care unit for a few days, then down to the intermediate care unit, and perhaps home from this area or back to the self-service unit once again before he went home. As another instance, a patient with diabetic coma was cared for in the special care unit and, as the diabetes and intercurrent complications were corrected, moved through the various phases of care to the self-service unit, where he completed his hospital stay. He finally went home after being sufficiently trained to care for his needs during his illness. These two brief examples point out the potentialities and flexibility of progressive patient care which answer the patient's needs.

After three months of operation, the Public Health Service became interested in the program and instituted a study committee to evaluate the effects and changes involved. These studies are still under way. At the time of this writing they include a study of costs and an evaluation of bed allocations. Results are to be reported soon. The total operation of the program, however, continues to be developed and directed by the hospital without the benefit of outside funds. The tremendous help of the Public Health Service in certain fields, such as the reorganization of the record department, must be recognized.[4]

Another benefit used in developing the program was "convincement by involvement." Sir Leslie Stephens has said: "The only way in which one human being can properly attempt to influence another is by encouraging him to think for himself instead of endeavoring to instill ready-made opinions into his head." We can expect a program to win acceptance when all the persons involved are given a chance to participate in the planning. If changes occur at the hands of highly respected persons whose leadership is established, the transition is more easily made. Being largely creatures of habit we all tend to take the line of least resistance. Once the force of inertia is broken, the changes follow easily. And, finally, most of us accept changes more gracefully if we feel we are consulted first; if we find we are active participants and not mere pawns in the situation. Hospital trustees, administrators, nurses, and medical staff should be involved in the planning stages right from the beginning.

And now, what about patients? Most patients will accept new ideas if they are adequately explained by their personal physicians. Patients say they feel promoted as they move from the special care unit to the intermediate care unit to the self-service unit and home. The physical progress becomes a symbol of their medical progress in overcoming disease. One can see that a patient normally faces a series of psychological adjustments during hospitalization. As a "sick" man he resigns his own will and allows others to make decisions for him. Later he gradually sloughs off this dependency state, becomes convalescent, and finally resumes the responsibility of his own care. The physical movement of the patient from nursing unit to nursing unit within progressive patient care acts as a stimulus to these psychological adjustments. It symbolizes to all concerned—doctor, nurse, family, and patient—that the patient's status is now changed and it is easier for him to overcome his former dependency and take the next step forward.

From the nurses' standpoint progressive patient care allows the nurse to work in the area for which she is best qualified. The nurse who enjoys the challenge of the life-and-death tension of the special care unit may welcome such an assignment. The nurse who enjoys teaching and talking with people might be happy on the self-service unit. The nurse who loves to mother and care for the long-term patient finds her niche in the continuation care unit, while the intermediate care unit offers a variety of care for the nurse who likes change.

What about the ledger sheet and costs? The philosophy of progressive patient care indicates that costs and charges should be equal and we should pass on to each patient his proportionate share of the expense of his hospitalization. At the time of this study, room, board, and nursing charges were as follows: special care unit $26 per day; flexible zone $20 per pay; intermediate care unit $18, semiprivate; and self-service unit $11, in the original experimental unit.

The costs either to the hospital or to the patient under progressive patient care are no greater and, indeed, evidence suggests that they are less. The patient who goes to the special care unit saves a large portion of the fee involved in paying private duty nurses ($54 per day in our area). The self-service unit allows us to return a surplus of $1 to $4 per day to Blue Cross on their average allowance in Connecticut of $12 and $15 per day for day-rate services. Further evidence of increased efficiency is revealed in studies of discharges per bed per year. The state average is 41, while at Manchester Memorial Hospital for 1957-1958 it was up to 51. The average patient stay for the state was 7.6 days, while at Manchester Memorial Hospital it was 6.4 days for 1957-1958.

A research comparison with 17 other hospitals of comparable size reveals that we employ fewer employees per hospital bed and pay higher wages and salaries. The total patient cost per day is 20% less than the average of the 17 other hospitals. These factors are particularly significant if one examines the room, board, and nursing care statistics which make up the largest portion of the patient's bill. In 1956, prior to the program of progressive patient care, the Manchester Memorial Hospital averaged 3.2 total hours of nursing care per patient during a 24-hour period. In April, 1959, the Manchester Memorial Hospital averaged 4.6 total hours of nursing care per patient during a 24-hour period. The breakdown of nursing time required by units revealed: special care zone, 6.3 hours; intermediate care unit, 3.9; self-service unit, 2.5; continuation care unit, 7.5; obstetrics, 3.7; and pediatrics, 3.7. In spite of obvious increases in the nursing staff under progressive patient care the salaries of our nurses were raised 32 cents an hour and currently are basically higher than any nonprofit voluntary hospital in the state. It is also significant that room, board, and nursing care average cost per case for the fiscal year 1958 was $106—a cost which is 20% less than the average cost of room, board, and nursing care in the other 17 hospitals.

These are all suggestive figures, but, since the program as instituted has been of a preliminary nature, it is necessary to develop adequate areas, particularly in the self-service unit, before the true picture can be evolved. The figures must be evaluated with caution. However, the objective of better patient care has been achieved—and at no greater cost to the patient.[5]

Comment

The hospital survived the reorganization operation and has continued to improve during the past two years. The stack of mail on the administrator's desk has changed from letters of criticism to letters expressing approval and satisfaction. The griping in the doctors' lounge has simmered down to an occasional case of flatulence. The nurses have been more content with the knowledge that their individual abilities are being utilized. The trustees noted with approval the black ledger sheet. In other words, the hospital has recovered. The prognosis is excellent.

Summary

The case report of a 39-year-old hospital in New England is presented with the hope that it might be of help to those who would care to treat similar hospital problems. There apparently are several basic procedures of value in treating a situation of this type. It is necessary that there be included an organization composed of all the power elements of the hospital, i. e., physicians, trustees, administrator, nurses, and, in larger institutions, representatives of nursing or medical schools to coordinate their various activities. Other basic ingredients are work and thought. A view of units already in operation may save much time and sad experience. An evaluation of the institution—a physical examination if you will—is necessary to determine the areas available for adaptation to the program. An evaluation of the patient load should be done to determine the number of the particular types of patients to be treated in each unit. After an adequate plan is developed, it should be approved by the medical staff, trustees, and other involved groups. With the cooperation of the medical staff and other groups of the hospital assured, the program may be instituted.

Problems which develop as the program progresses are documented, reported, and resolved at the level of the unit committee. There is no "passing the buck." Radical changes in the physical plant are probably best delayed until experience has been gained as to function and capacity of each unit. Then, with adequate experience the proper areas may be designed and developed. Consultants of business research orientation have proved to be of considerable help in evaluation of various problems. As with any large industry (hospitals are now the third largest industry in the United States) a certain amount of funds should be invested in basic research each year in order to improve the product—otherwise it remains static. This remains the plight of many hospitals today.

The primary tenet, however, must remain a consideration of each individual patient and his medical needs. By segregating patients through a systematic classification of similar medical needs, detailed studies of their respective problems and definite answers to the problems become possible. Variations of the indicated techniques should be applied to satisfy the particular needs of each individual hospital. Progressive patient care thus becomes a method of providing better patient care.

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SUBACUTE BACTERIAL ENDOCARDITIS IN THE OLDER AGE GROUP

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In a series of 55 patients with subacute bacterial endocarditis there were 18 aged 50 years or older. The diagnosis was based either on autopsy findings or on the presence of typical signs and symptoms and positive blood cultures. In 3 of the 18 no heart murmurs were detected during life, and even in retrospect adequate clinical criteria were lacking, so that the diagnosis became clear only at autopsy. The atypical nature of many cases resulted in confused diagnoses and misdirected treatment. This was the most common reason for mortality. Thirteen (72%) of the 18 older patients died. Among the 37 younger patients only 10 (27%) died. Reasons are given for believing that mortality from this disease in older people can be substantially reduced if the disease is watched for and properly treated.

Today, subacute bacterial endocarditis is one of the few nonsurgical cardiac diseases which can be cured. In this antibiotic era it has been estimated that mortality due to this disease should be no more than 5%,[1] whereas in actuality the death rate has been reported to be between 20 and 40%.[2] In various series[3] the mortality in the aged has been strikingly higher than in the younger age group. It has even been stated that the mortality and morbidity due to this disease increase significantly in patients past 30 years of age.[2b] With an increasingly aging population, and with subacute bacterial endocarditis no longer considered a rarity in the older age group,[4] it becomes important to attempt to elucidate the nature of this condition in the older age groups and especially to investigate the causes for the increased mortality.

Patients

The Montefiore Hospital maintains ward and private beds for the treatment of acute and long-term illness. From 1945 to 1955, 55 cases of subacute bacterial endocarditis were seen at this institution. The diagnosis of endocarditis was proved either on the basis of autopsy findings or by typical signs and symptoms substantiated by positive blood cultures.

Age distribution did not differ significantly from other reports.[5] Of the 55 cases, 18 patients, or 32%, were aged 50 years or older and constituted the basis for this report. One patient (cases 2 and 5

From the Medical Division, Montefiore Hospital.

in table), aged 60, had two episodes of subacute bacterial endocarditis with different organisms during a 10-month interval. Each attack is considered separately.

Diagnostic Criteria

The murmur of a valvular defect or congenital lesion, febrile course, embolic phenomena, and positive blood culture are the accepted criteria and were considerably lower in those patients in the group aged 50 years and older.[6] The cases of subacute bacterial endocarditis in the older age group may be subdivided into three clinical groups as follows:

Group 1.—Six patients (cases 1 to 6) had well-defined symptoms that conformed to the criteria of Libman and Friedberg as listed above.[6] Clinical suspicion led to the confirmation of the diagnosis by positive blood culture.

Group 2.—Five patients (cases 7, 8, 9, 10, and 11) had murmurs, fever, and/or anemia as the only signs of endocarditis. Four out of five of these patients had blood cultures drawn repeatedly. All cultures were negative; the diagnosis of subacute bacterial endocarditis was discarded and another diagnosis was considered to explain the symptoms. (For details see table.)

Included in group 2 were three patients without murmurs (cases 12, 13, and 14). The major clinical problems in these cases were as follows: One patient (case 12) had congestive heart failure of unknown etiology, another (case 13) had multiple neurological signs and symptoms, and the third (case 14) had a pleural effusion of undetermined etiology.

Group 3.—Four patients had another active disease (cases 15, 16, 17, and 18). One patient (case 15) had a cerebrovascular accident, genitourinary infection, and prostatic obstruction; one (case 16) had myocardial infarction and prostatic obstruction; one (case 17) had a fractured hip, infected decubitus ulcers, and pyelonephritis; and the fourth (case 18) had carcinoma of the lung and prostatic obstruction. In all of these patients the symptoms could have been explained by diseases other than subacute bacterial endocarditis.

Therapy

Of the 18 patients in the older age group, only 6 were treated in Montefiore Hospital. All were in group 1 of our criteria for diagnosis, and the common diagnostic criteria were present. Five recovered; the sixth died from an enterococcic organism that was resistant to treatment with penicillin. Of the survivors, four had infection with Streptococcus viridans and one with gamma hemolytic streptococcus. These infections responded to penicillin therapy.

The average dosage of penicillin used was 12 million units per day. The highest dose was 14 million units per day for 51 days and the lowest dose was 600,000 units per day for 22 days. In all cases but one, aqueous penicillin was used. The one exception was the instance cited above as the "lowest dose" case, in which a long-acting penicillin preparation was used.

Of the 37 patients with subacute bacterial endocarditis in the younger age group, 31 received adequate penicillin or other antibiotic therapy. Of the treated patients, 27 recovered and 4 died. The older age group, properly treated, did as well as the younger age group.

Mortality

Of the 55 patients in both age groups, 23 died from their disease, an over-all death rate of 42%. Thirteen of the 18 older patients died, a death rate of 72%. Of the 37 patients under 50 years of age, 10 died (mortality of 27%). A total of 31 men and 24 women were included in this series. Fifteen men died, as opposed to eight women. This ratio was the same in both older and younger age groups.

Causes of Death

Death due to subacute bacterial endocarditis most commonly falls under three categories:

Failure of Treatment.—There may be failure of treatment, which in turn may be due to the use of the wrong antibiotic, inadequate dosage, or a resistant organism. One of our older patients (case 5) was in this group. The organism was a penicillin-resistant enterococcus.

Diagnostic Errors.—There may be an error in diagnosis, either with or without the presence of adequate criteria for the diagnosis of subacute bacterial endocarditis. (See criteria for diagnosis in group 2.)

In four of these patients the diagnosis of subacute bacterial endocarditis was suspected but was discarded because of repeatedly negative blood cultures, one patient (case 7) having had 15 negative cultures. One of these patients (case 8) had been treated at another hospital for subacute bacterial endocarditis, and after seven negative blood cultures at Montefiore Hospital the patient was not considered to have active disease. In case 9, despite the recent onset of clubbing and the presence of anemia and heart murmurs, the diagnosis of subacute bacterial endocarditis was discarded and that of pyelonephritis was made. Pyelonephritis was found on postmortem examination, but so was subacute bacterial endocarditis. A history of cancer of the breast 17 years before and four negative blood cultures led to a diagnosis of metastatic cancer in the patient in case 10. At autopsy no cancer was revealed, only subacute bacterial endocarditis. The severe anemia in case 11 led to a diagnosis of hemolytic anemia which was treated with steroids. No blood cultures were drawn.

In three patients (cases 12, 13, and 14), even in retrospect, adequate criteria for the diagnosis of subacute bacterial endocarditis were not present. In none were murmurs detected during life. In

Summary of Eighteen Cases of Subacute Bacterial Endocarditis in Older Age Group

Case, No.	Age, Yr.	Sex	Chief Symptoms	Fever	Murmur	Clubbing	Splenomegaly	Embolism	Hemoglobin Level, Gm. per 100 Cc.	Blood Cultures	Postmortem Findings	Comment
1	60	F	Anemia; weakness	+	Systolic at base	...	+	...	9.5	Str. viridans 2/2	...	Cured; died 4 yr. later of congestive heart failure; postmortem findings showed old rheumatic valvulitis; healed focal glomerulonephritis; healed subacute bacterial endocarditis
2	60	F	Pallor; weakness	+	Systolic at apex; diastolic at base	...	...	+	11	Str. viridans 5/5	...	Cured; later recurrence with another organism (case 5)
3	66	M	Congestive heart failure	...	Systolic and diastolic at apex and base	...	+	+	12.8	Str. viridans 5/1	...	Diagnosis made on basis of murmurs, splenomegaly, and one spot; cured
4	63	M	Pallor; weakness; cerebrovascular accident	+	Systolic and diastolic at apex	...	+	+	10.5	Gamma hemolytic streptococcus 3/3	...	Admitted as diagnostic problem; murmurs detected after admission leading to search for subacute bacterial endocarditis by multiple blood cultures; cured
5	60	F	Fever of undetermined origin	+	Systolic at apex and base	...	...	+	11	Str. liquifaciens 6/1	...	Same patient as case 2; recurrence of subacute bacterial endocarditis with a 2nd organism; treated with 9 × 10^6 units of penicillin, 36 Gm. of streptomycin 1.6 × 10^6 units of bacitracin in 2 wk. time; treatment failure; died
6	53	F	Chills	+	Diastolic at apex	...	+	...	10	Str. viridans	..	Cured; associated diabetes mellitus; positive cultures present at another hospital
7	55	F	Cough; abdominal pain	+	Systolic at apex; diastolic at apex	+	+	+	10.5	15/0	Rheumatic heart disease; subacute bacterial endocarditis, aortic valve	Diagnosis not made; treatment for active rheumatic fever with ACTH
8	52	M	Weakness	+	Systolic and diastolic at base	...	...	+	12	7/0	Healing subacute bacterial endocarditis and multiple emboli	Treated at another hospital with 3 billion units of penicillin in 3 mo.; considered cured in Montefiore Hospital and no treatment given
9	58	F	Weakness	...	Systolic at apex and base; diastolic at apex and base	+	...	..	9	2/0	Subacute bacterial endocarditis; aortic valves ruptured	Diagnosis not made; pyelograms made; anemia thought due to renal infection; died with anuria
10	61	F	Weight loss	+	Systolic and diastolic at base; systolic at apex	...	..	...	8	4/0	Rheumatic heart disease with mitral insufficiency, mitral stenosis, aortic insufficiency, and aortic stenosis; subacute bilateral endocarditis; spleen weighed 300 Gm.; no cancer found	Known rheumatic cardiac; cancer of breast with mastectomy 17 yr. prior to admission; illness considered metastic cancer and treated as such; 4 blood cultures drawn, all negative
11	82	M	Congestive heart failure; abdominal pain	...	Systolic and diastolic at base	...	...	...	8.5	None drawn	Arteriosclerotic heart disease, vegetation on aortic cusp with rupture of cusp; benign prostatic hypertrophy; renal calculi	Clinical problem, congestive heart failure; anemia of unknown etiology; treated with steroids for hemolytic anemia
12	77	F	Weakness; cough; congestive heart failure	...	...	...	...	...	16.5	None drawn	Healed rheumatic heart disease, mitral subacute bacterial endocarditis; arteriosclerotic heart disease with no coronary occlusions	History of "rheumatism" at 34 yr. of age; admitted primarily for treatment of congestive heart failure; no clinical criteria to suggest subacute bacterial endocarditis
13	65	M	Cerebrovascular accident	...	...	...	...	...	9	None drawn	Mural thrombus left ventricle, infected with hemolytic Staph. aureus, beneath the thrombus, heart muscle thinned and scarred; emboli to brain, kidney, adrenals	Clinical picture dominated by neurological signs and symptoms; onset with recurrent episodes of diplopia, headache, vertigo; developed right homonymous field defect, 3 spinal taps, negative; eosinophilia 62%; treated with ACTH for possible periarteritis; died 4 mo. after onset, no involvement of valves of heart; no clinical reason to suspect subacute bacterial endocarditis
14	57	F	Cough and hemoptysis	•	...	...	...	...	13.5	None drawn	Rheumatic heart disease; subacute bilateral endocarditis	Diagnosis of cancer of lung because of pleural effusions, cell block of fluid negative

Summary of Eighteen Cases of Subacute Bacterial Endocarditis in Older Age Group—Continued

Case. No.	Age, Yr.	Sex	Chief Symptoms	Fever	Murmur	Clubbing	Splenomegaly	Embolism	Hemoglobin Level, Gm. per 100 Cc.	Blood Cultures	Postmortem Findings	Comment
15	57	F	Cardiovascular disease; genitourinary infection	...	Systolic and diastolic at base; systolic at apex	+	...	...	10.5	None drawn	Rheumatic heart disease; ruptured aortic valve; cancer of prostate with metastases to lung	Diagnosis not suspected of primary infection; treated for urinary infection; prostatic cancer not suspected
16	72	M	Weakness; weight loss	...	Systolic and diastolic at base	...	...	...	10	None drawn	Aortic stenosis; myocardial infarction; subacute bilateral endocarditis with mycotic aneurysm of aorta	Subacute bilateral endocarditis not suspected; prostatic obstruction; death due to myocardial infarction secondary to coronary occlusion
17	70	M	Fractured hip and decubitus ulcers	+	...	...	...	...	10.4	Proteus vulgaris	Fractured left hip; pyelonephritis and renal calculi; decubitus ulcers, arteriosclerotic heart disease; subacute bilateral endocarditis with vegetation on aortic valve	Fractured hip with decubitus ulcers and pyelonephritis which could explain fever, anemia, and + blood culture; died 2 days after start of antibiotic therapy
18	77	M	Pallor; weakness; obstructive uropathy	..	Systolic at base	...	...	...	6	None drawn	Anaplastic cancer, right upper lung with metastasis to liver; subacute bacterial endocarditis	Admitted primarily for benign prostatic hypertrophy; benign prostatic hypertrophy and obstructive uropathy; cancer of lung found on routine x-ray; little to suggest subacute bacterial endocarditis which was not suspected

* Occasional spike in hospital.

two, however, definite healed rheumatic valvular disease was found on postmortem examination.

Associated Disease.—There may be associated disease. Four patients, (cases 15, 16, 17, and 18) had several other clinical conditions that dominated the picture, so that the diagnosis of subacute bacterial endocarditis was not suspected. These associated diseases were of such a serious nature that they led to the death of the patients. Pyelonephritis, with or without obstructive uropathy, was present in each of these cases and satisfactorily explained much of the clinical picture.

Of the 10 patients under 50 years of age who died, in 4 death was due to failure of treatment. In the other six, the diagnosis was not suspected. Of the 13 fatalities in patients over 50 years of age, 12 died without a clinical diagnosis of subacute bacterial endocarditis.

Comment

In order to establish the diagnosis of subacute bacterial endocarditis in the older age group, it must first be suspected. At one time considered sufficiently rare to comment on,[7] this entity is now accepted as being not uncommon in the elderly. However, there is agreement that the diagnosis can be difficult to make.[8]

The question arises as to what constitute adequate clinical signs for the diagnosis of subacute bacterial endocarditis. The original criteria of Libman and Friedberg are familiar.[6] Later, Friedberg [1] recommended that fever of more than one week's duration in a person with a heart murmur should lead to a suspicion of subacute bacterial endocarditis. Parsons and co-workers [9] pointed out the significance of anemia in the presence of a heart murmur as a clue to the diagnosis of subacute bacterial endocarditis.

In the older age group, diagnosis offers special problems. Murmurs are common but they may be disregarded. Fever may be attributed to other conditions, notably bronchopneumonia or urinary tract infection.[10] Anemia may be dismissed as being of nutritional origin. Weakness and pallor are nonspecific complaints. Also, the clinical signs are often of insidious onset [3a] and much less accentuated than in the younger patient.[3b] Finally, subacute bacterial endocarditis may occur in the presence of another disease. The other disease can in itself account for many of the usual signs of endocarditis. In such instances diagnosis is most difficult to make.

Recently, Wallach and co-workers [11] have pointed out that bacterial endocarditis in the elderly often complicates other diseases and is frequently a terminal event. In these instances the bacterial endocarditis was acute and not subacute. Zeman and Siegel [4a] feel, however, that subacute bacterial endocarditis is more common in the elderly than acute bacterial endocarditis and is a terminating rather than a terminal event and that proper diagnosis and treatment can prolong life. In our cases, all had subacute bacteria endocarditis, and it is felt that this condition could not be considered a terminal event.

In order to decrease mortality from subacute bacterial endocarditis in the older age group, a correct diagnosis must be established more frequently. No murmur should be disregarded. Weakness, anemia, and low-grade fever should lead to a suspicion of subacute bacterial endocarditis when not clearly explained by another cause. Even in the absence of a positive blood culture, treatment should be instituted whenever the diagnosis of subacute bacterial endocarditis is seriously considered. Subacute bacterial endocarditis can be suspected even in the presence of an associated disease. When an older patient with heart murmur, fever, and anemia fails to respond to apparently adequate therapy, subacute bacterial endocarditis should be considered.

Summary

Eighteen cases of subacute bacterial endocarditis, in patients aged 50 or older, are presented as part of a series of 55 cases in all. Mortality in the older age group was 72%, as opposed to 27% in the younger age group, seen at the same institution during the same period of time. The failure to make a proper diagnosis of subacute bacterial endocarditis and therefore lack of proper treatment was the most common cause of increased mortality in the older age group. Properly treated, the disease was cured in five out of six cases in the older age group.

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OSCILLOMETRIC ARTERIAL CIRCULATORY NORMS

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Oscillometric measurements were made in 12 healthy men and were used to calculate oscillometric indexes at six levels from the instep of the foot to the upper part of the thigh. This made it possible to systematize the interpretation of data from the increasing numbers of patients (330 in 1958) whose peripheral vascular status must be evaluated at the request of medical and surgical services. Three case histories, involving men aged 53, 58, and 71 years, illustrate the application of the six indexes in determining the level and extent of vascular occlusions. These results not only help to determine the type of operation needed but also serve as criteria for subsequent improvement in the patient.

One of the fundamentals in medicine is to have objective "normal values" so we can detect the abnormal. Such norms are lacking for the peripheral arterial circulation. With the increasing incidence of peripheral arterial circulatory disorders, it becomes important to have norms in order to detect the early onset, to follow the progress of the disease, to evaluate medical as well as surgical methods of treatment, and for differential diagnosis.

Many methods have been proposed and are used to evaluate the state of the peripheral arterial circulation, especially in the lower extremities. Some of these methods are palpation of the arteries, determination of claudication time, determination of venous filling time, skin temperature measurements, plethysmographic measurements, oscillomet-

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ric testing, and arteriograms. Of these, arteriograms have been most universally accepted as reliable. However, arteriograms are surgical procedures, requiring special techniques and equipment, making them impractical except in selected cases. Of the other methods, none is satisfactory, but evaluation with the oscillometer is gaining increasing recognition. The oscillometer was originally designed for the measurement of blood pressures. The best known instrument is that designed according to the principles of Pachon.[1]

After the invention of this instrument by Pachon, it was soon noticed that it could be useful in peripheral arterial vascular work. Samuels is credited with having introduced the oscillometer in the United States in 1927. Since then opinions about its usefulness have varied. Samuels[2] stated: "For accurate quantitative measurement of arterial pulsations, an oscillometer is indispensable." Wright[3] stated: "The oscillometer may be a valuable aid in the hands of one who understands the evaluation and interpretation of the findings." Allen and colleagues[4] stated: "Although we have found the machine useful for recording of the pulsations in the extremities, for publication of data, for future reference, and for teaching purposes, in our experience it has been one of the least valuable of all methods of investigation of the peripheral circulation." Collens and Wilensky[5] stated: "The oscillometer is probably one of the most valuable instruments available for determining the degree of arterial obstruction through a limb." Chandler and Dickinson[6] stated: "Its use should be primarily experimental, and clinical judgment should take precedence in arriving at decisions about treatment."

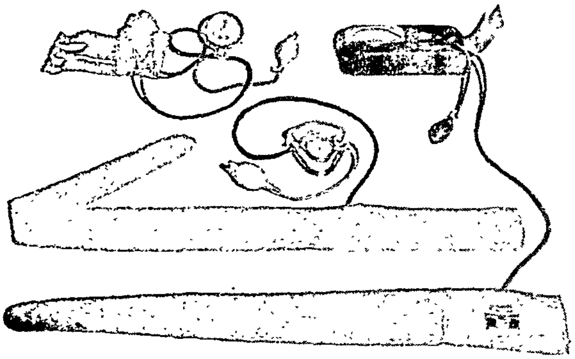

Fig. 1.—*Upper left,* Von Recklinghausen type of oscillometer, made in Germany. *Upper right,* oscillometer made in United States on Pachon principle. *Center,* Pachon type of oscillometer, made in Germany and used in this work. All three show different readings.

There is thus a variety of opinions about the usefulness of the oscillometer. The first reason for this is that there are many different types of oscillometers. Each type will give a different reading, depending on the construction of the instrument, the cuff, and the tubing. An electronic oscillometer will show a high reading, while a mechanical one will show a low one. Thus, investigators cannot compare results unless they use the identical type of oscillometer. It is not like the mercury-type sphygmanometer, in which all factors are constant and one model of which in New York will give the same readings as one in Minneapolis.

The second reason for the divergence of opinion is that there is a lack of norms for comparison. A blood cell count would similarly be useless if we did not have a "normal blood cell count" to compare with it. To make the oscillometer really useful requires that the same instrument be used all the time and that norms be developed for that instrument.

Absence of norms has been recognized. Atlas[7] in 1939 proposed that, with use of an oscillometer to evaluate the arterial circulation, the ratio between the oscillometric index at the lower leg and that at the lower part of the forearm be used to detect early arteriosclerosis. The ratio should normally be "one" and if lower would indicate decreased arterial pulsations in the lower leg. However, this norm depends on the circulation in the forearm, and when that is decreased, as is often the case, then the ratio will not hold. Furthermore, we need norms not only in the lower leg but also in the foot, in the upper leg, in the thighs, and in the upper extremities. Thus, the norm proposed by Atlas, while a step forward, does not solve the problem.

In 1951, I[8] proposed that the evaluation of the arterial circulation in the legs would be on the basis of the following three points: (1) the resting circulatory requirement; (2) basic walking requirement; and (3) amputation site requirement. Refinement and extension of this work was reported in 1958,[9] detailing the norms arrived at for the circulation below the knees. The work to be reported here is a further development of norms for the circulation in the thigh and a check on the clinical reliability and value of these norms.

A Pachon type of mechanical oscillometer (fig. 1) has been constantly used in this work with a specially designed cuff. This is done for the purpose of eliminating as many variables as possible. Readings have been taken in the supine resting position, beginning at the instep, then above the ankle, below the knee, above the knee, in the middle of the thigh, and in the upper thigh, at specified landmarks. The rubber cuff has been inflated to 140 mm. Hg and then gradually allowed to deflate 20 mm. Hg at a time until it returns to zero. The greatest excursion of the needle, called the oscillometric index, has been noted. This excursion occurs when the pressure in the cuff is barely sufficient to overcome the tissue resistance under the cuff plus the diastolic pressure in the arteries. The arteries are compressed at this point. When the systole occurs the arteries are opened up by the pulse pressure. This displaces air in the cuff, forcing the diaphragm in the oscillometer to expand. The needle connected to the diaphragm will express by its excursion the total systolic peak capacity of the arteries in the segment under examination.

Two clinically useful norms were established for the arterial circulation below the knee. The first norm was established by measuring a group of adult males with cyanosis of the toes or minimal gangrene. It was found that there was only a minimal variation in the readings and that, with an oscillometric index of "0" at instep, "0" above ankle, and one-eighth of a point below the knee, there is imminent danger of spontaneous gangrene for lack of arterial circulation. This norm can be called the gangrene point.

The second norm can be called the walking norm or the lower limit of normal. This norm was obtained by testing a group of patients complaining of claudication at distances varying from an average of 95 steps to 420 steps. It was found that the oscillometric index increased as the walking distance increased. By plotting curves and carrying curves to 500 steps, walked in a specified manner, oscillometric indexes were obtained for this distance. The norms for this distance were expressed by an oscillometric index of 0.5 at instep, 2.5 above the ankle, and four below the knee. With these readings a patient should be able to walk 500 steps, each step 30 in. long, at a rate of 120 steps a minute on a linoleum floor while wearing shoes.

The norms that were developed proved reliable in evaluating the arterial circulation below the knees. However, it is equally important to have norms for the arterial circulation in the thighs, because most obstructive processes in the arteries occur above the knees. Norms for the thigh circulation were established in the following manner. The average oscillometric index was determined in 12 healthy males, aged 21 to 69 years, weighing 135 to 205 lb. (61 to 93 kg.). It was found to be as follows: instep 0.75, above the ankle 4, below the knee 7, above the knee 5.5, middle of the thigh 4, upper part of the thigh 4.5.

The "lower limit of normal" oscillometric index as previously established below the knee is as follows: instep 0.5, above the ankle 2.5, and below the knee 4. This is a 40% reduction of the leg index for healthy adult males. If this reduction is applied to the thigh figures for healthy adult males, then we get a lower limit of normal for the thigh vessels as follows: above the knee 3.3, middle of the thigh 2.4, and upper part of the thigh 2.7. It must be constantly borne in mind that these figures represent the lower limit of normal and that they are not absolute. When the lower limit of normal has been reached, there is already some degree of vessel obliteration present.

With the knowledge that absolute precision cannot be obtained, the thigh index was changed to the nearest half. The complete lower limit of normal index for the lower extremity in the adult male then became as follows: instep 0.5, above the ankle 2.5, below the knee 4, above the knee 3.5, middle of the thigh 2.5, upper part of the thigh 2.5. These figures are now used in evaluating the arterial circulation in the lower extremities. The figures apply only to the type of oscillometer used, a Pachon type, and not to others. After a test has been done and reduced indexes found, the indexes are converted into a percentage loss below the lower limit of normal. This method of evaluating the arterial circulation has now become routine in practically every person suspected of having peripheral vascular disease. Its usefulness is attested by the increasing numbers of tests done at the Minneapolis Veterans Administration Hospital each year. In 1954, there were 52 oscillometric evaluations. In 1955, there were 123. This number increased to 200 in 1956, to 289 in 1957, and to 330 in 1958, all patients having been referred for evaluation by the medical and surgical services.

To check the accuracy of the interpretation, many tests were correlated with arteriograms, operative findings, and pathological reports. The accuracy of the test was found to be quite satisfactory. It was especially noted how valuable the oscillometric norms could be in locating not only the level but also the degree of occlusion in the lower extremities and, with experience, in the abdominal vessels and the aorta to a high degree of accuracy. The following cases illustrate not only how the level of occlusion is determined but how the degree of occlusion is arrived at on the basis of the oscillometer norms.

Report of Cases

CASE 1.—A 71-year-old man had had a nonhealing injury of his right foot for eight months. The oscillometric index was as follows: right instep 0, above the ankle 0.25, below the knee 2.5, above the knee 7.5. Compared with the lower limit of normal, this constituted a 100% loss at instep, a 90% loss above the ankle, and a 40% loss below the knee. Above the knee, the reading was 7.5, or almost twice the lower limit of normal. The conclusion was drawn that the arteries were wide open above the knee; below the knee there was a partial obstruction, becoming practically complete between the knee and the ankle.

The arteriogram (fig. 2) showed good filling of the popliteal artery, except at its lower end, where beginning sclerosis was evident, increasing in the anterior and posterior tibial arteries, and in the peroneal artery. In the middle of the calf, the filling was poor, and it was still less in the lower third.

At operation there was good pulsation in the popliteal artery. The peroneal and the tibial arteries were largely sclerotic, with no blood flow through the peroneal. The posterior tibial artery showed a fair amount of bleeding.

The pathological report showed severe sclerosis and narrowing of the posterior tibial, peroneal, anterior tibial, and dorsalis pedis arteries. Sections revealed that they were nearly occluded by atheromatous fibrous deposits.

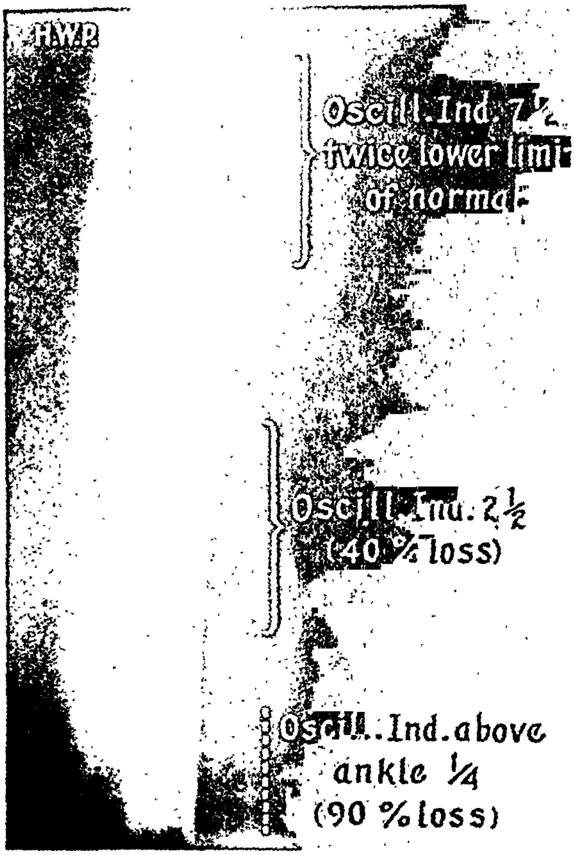
HWP
Oscill.Ind. 7½ twice lower limit of normal
Oscill.Ind. 2½ (40% loss)
Oscill.Ind.above ankle ¼ (90% loss)

Fig. 2.—Loss of arterial circulation as estimated by use of oscillometric norms corroborated by appearance of arteries in arteriogram. Operative and pathological findings further confirmed oscillometric evaluation.

Case 2.—A 58-year-old man had had a nonhealing ulcer of the left ankle for over three years. The oscillometric index was as follows: left instep "trace" (95% loss), above the ankle 0.125 (95% loss), below the knee 0.125 (95% loss), above the knee 0.25 (90% loss), middle of the thigh 2.25 (10% loss), and upper part of the thigh 2.5 (lower limit of normal).

The sharp drop from 2.25 in the middle of the thigh to 0.25 above the knee indicates a complete occlusion in the lower third of the thigh.

The arteriogram showed filling of the femoral artery in the upper part of the thigh with gradual narrowing of the lumen progressively down the thigh. At the junction of the middle third of the thigh with the lower third, there was a complete occlusion (fig. 3).

The pathological examination revealed the popliteal artery to be thick, atherosclerotic, and calcified. The lumen was completely obliterated by organized thrombus, with a few residual channels running through the thrombus.

Case 3.—A 53-year-old man developed back and leg pains 16 years ago after a back injury. The pains were ascribed to a herniated disk, but he was never operated on. Eight years ago he noticed tiredness in his legs, but he ascribed it to his back. Gradually the tiredness increased, and one year ago he had to stop working.

The oscillometric index was as follows: left instep 0.125 (75% loss), above the ankle 1.75 (30% loss), below the knee 2.75 (30% loss), above the knee 2.75 (30% loss), above the knee 2.5 (30% loss), middle of the thigh 1.5 (40% loss), and upper part of the thigh 2 (20% loss); right instep 0.12 (75% loss), above the ankle 1.5 (40% loss), belo the knee 3 (30% loss), above the knee 2 (20% loss) middle of the thigh 1.5 (40% loss), and upper par

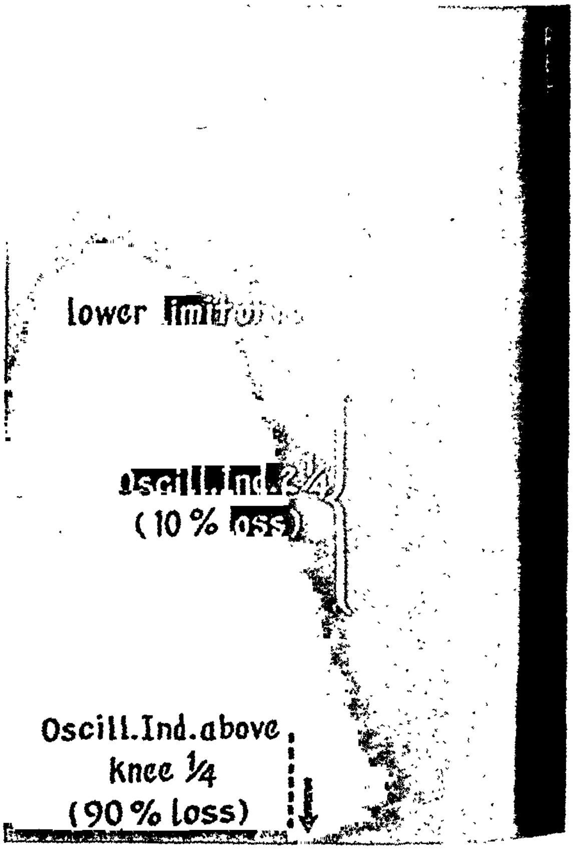

Fig. 3.—Case of nonhealing ulcer of left ankle for three years. Oscillometric test indicated complete occlusion of arteries in lower third of thigh. Arteriogram and pathological findings confirmed this.

of the thigh 2 (20% loss). The equal loss in the upper parts of the thighs indicated an aortic obstruction.

Aortography revealed (fig. 4) the aorta visualized from the level of the renal arteries to its bifurcation into the iliac arteries. The entire portion of the aorta showed evidence of atherosclerosis which was particularly marked just above its bifurcation.

At operation, a normal pulse rate was found in the middle of the abdominal aorta, but the terminal aorta, especially to the left, was filled with atheromatous plaques and the pulsation was much diminished. Thromboendarterectomy was done.

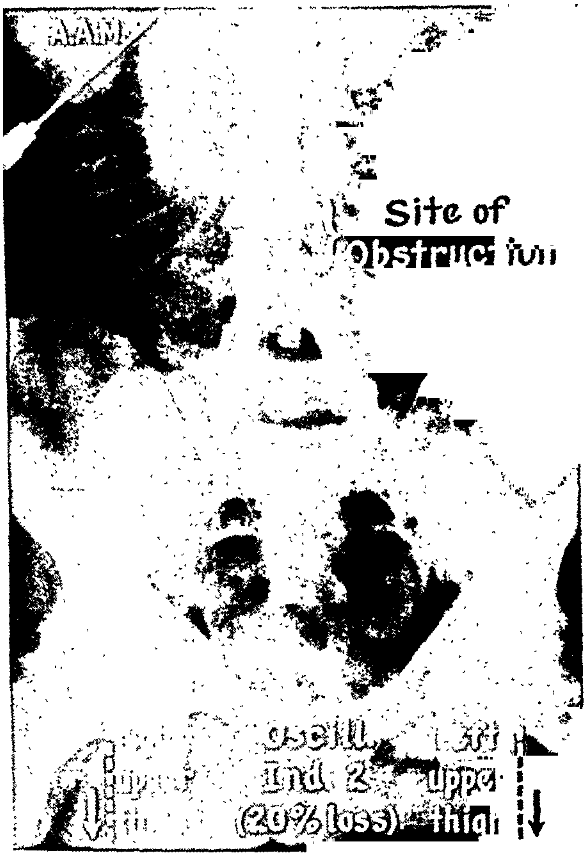

Fig. 4.—Aorta from level of renal arteries to bifurcation into iliac arteries. Oscillometric test of patient with leg tiredness of eight years' duration and ascribed to old back injury showed equal loss in both thighs and indicated partial obstruction in aorta, later confirmed by aortogram and operative findings.

Twenty days after the operation a follow-up oscillometric test was done. This showed a good restoration of the circulation to the lower extremities.

Summary

Objective clinical norms are lacking for the arterial circulation in the extremities. They are needed for the early detection of disease, to follow the progress of the disease, to evaluate medical and surgical treatment, for differential diagnosis, for medicolegal purposes, and in general for the same reasons as we need norms in other fields of medicine. Two clinically useful norms were established by the use of a standardized oscillometer. The first norm is called the gangrene point and is expressed by an oscillometric index of zero at the instep, zero above the ankle, and 1.125 below the knee. When these readings are present, then gangrene is imminent. The second norm can be called the walking norm or the lower limit of normal and is represented by readings of 0.5 at the instep, 2.5 above the ankle, 4 below the knee, 3.5 above the knee, 2.5 in the middle of the thigh and 2.5 in the upper part of the thigh. These readings should permit a walk of 500 steps, two long blocks, or one-fourth of a mile in a specified manner. These norms have been used to evaluate the arterial circulation in 994 cases in a period of four years and have been found to be reliable and useful. To test the reliability of the norms, many tests were checked with arteriograms, operative findings, and pathological reports. The norms can reveal accurately the degree and location of the occlusion. The oscillometer and the norms become invaluable in the examination and treatment of peripheral vascular cases. They can be used to detect the early cases of vascular disease, permitting early treatment and possibly the saving of many limbs. They provide an easy practical method of objective evaluation and a permanent record for the physician.

54th Street and 48th Avenue South (17).

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NONUROLOGIC SYMPTOMS IN PATIENTS WITH RENAL CANCER

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This study revealed that in one-third of a series of 577 patients with renal cancer the classic triad of symptoms—i. e., hematuria, flank pain, and flank tumor—was absent. On the other hand, they had one or more atypical or nonurologic symptoms such as fever, weight loss, and weakness. Pain was the chief complaint in 31 patients, but it was not in the flank. Twelve patients sought attention because of a painless tumor mass in the abdomen. There was absence of gross hematuria in 179 patients, and microscopic examination of the urine showed the absence of red blood cells in 109. The classic symptom-complex should always suggest renal tumor, but in the presence of atypical symptoms, not otherwise explained an intravenous urogram may reveal the hidden cause and thereby aid in earlier diagnosis. Metastases were demonstrated in 80 of the patients at the time of discovery of the renal neoplasm.

Creevy[1] in 1935 stated that "malignant renal tumors should be classed with syphilis and tuberculosis among the great mimics encountered in clinical medicine." In support of this statement, insofar as it applies to kidney tumors, are a number of reports ranging from the rare but intriguing association of renal neoplasms with tuberous sclerosis,[2] hemangiomatosis (Hippel-Lindau disease),[3] polycythemia,[4] and hypercalcemia (without evidence of bone metastasis)[5] to the more commonly observed yet atypical syndromes characterized by fever of unknown origin, unexplained weakness, anorexia, loss of weight, anemia, etc.[6] While most of the reports deal with, or emphasize, the puzzling association of renal neoplasms with certain lesions of the central nervous system or the hematopoietic organs, the more frequent symptom complex of fever, loss of weight, and weakness observed concomitantly with renal tumors is not stressed sufficiently. Thus, current textbooks[7] of internal medicine, surgery, or even urology either omit discussion of this atypical manifestation of renal cancer or discuss it only briefly. On the other hand, it has been reported[8] recently that 40% of one group of patients with renal carcinoma had fever.

The relatively common occurrence of atypical symptoms in patients with malignant renal neoplasms became apparent to us during the clinicopathological analysis of 577 consecutive cases of proved renal neoplasms in adults, seen at the Squier Urological Clinic at the Presbyterian Hospital, New York City, from 1930 through 1956. It was found that 183 (31.7%, or about one-third) of the 577 patients with renal cancer came with nonurologic or atypical symptoms. The majority of the 183 patients were admitted to the wards of the medical, neurological, or orthopedic departments because of cryptic fever, unexplained debility, and loss of weight; headaches, numbness, and weakness of the extremities; or sciatic pain and pathological fractures.

Numerous clinical and laboratory tests were performed and a variety of diagnoses proposed, such as lymphoma, multiple myeloma, tuberculosis, collagen disease, sarcoidosis, and amyloidosis. Usually a considerable period of time elapsed before the correct diagnosis was established. In a few instances the true nature of the disease was discovered only at autopsy. In some patients the diagnosis was made incidentally, either as a result of roentgenographic studies of organs or tracts other than the genitourinary system or after an intravenous urogram had been made, not infrequently, as a "shot in the dark."

Criteria for selection of patients included in this group with nonurologic or atypical symptoms were as follows: 1. Absence of hematuria. Any patient who complained of hematuria, even though he might have had fever, anorexia, or loss of weight, was excluded from this study. The only exception to this rule was the inclusion of four patients who had polycythemia associated with renal cancer and who complained of hematuria. 2. Absence of flank pain. Any patient who complained of flank pain, even though he also had fever and weakness, was excluded. On the other hand, patients with pain other than in the flank, such as in the chest, midabdomen, sacroiliac junction, and along the sciatic nerve, were included. 3. Absence of flank mass. Any patient with a flank mass, if the latter was accompanied by pain, even in the absence of hematuria, was excluded. But, patients with a painless flank or abdominal mass were included because in the majority of cases the masses were originally considered as splenomegaly, hepatomegaly, retroperitoneal tumor, etc., rather than renal enlargements.

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An exhibit based on findings in this review was presented at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 8-12, 1959.

Symptoms and Findings

In table 1 are listed, in order of frequency, symptoms and signs, as they were obtained from the group of 183 patients who qualified for this study. Weight loss, pain other than in the flank, weakness, anorexia, and fever were present in 95 (16.5%) of the total number (577) of patients with renal cancer (table 2). These symptoms, particularly if in varying combinations, were usually present in patients with metastases. Fever was a prominent symptom and occurred in patients both with and without evidence of demonstrable metastases.

As already mentioned, in 12 other patients a painless abdominal mass was found. The latter was discovered incidentally and interpreted as being due to conditions such as hepatomegaly, splenomegaly, and retroperitoneal neoplasms rather than to a kidney tumor.

Cough and dyspnea were recorded in 13 instances. These symptoms were usually present in patients with pulmonary metastases or cardiac failure.

There was a group of 10 patients who came primarily because of symptoms and signs of prostatism, but during their preoperative evaluation the intravenous and/or retrograde pyelogram disclosed the presence of the "hidden" renal tumor.

Hypertension was the chief complaint in eight patients who, with two exceptions, had generalized arteriosclerosis in addition to the neoplasm of the kidney. In only one patient, a 50-year-old male, did the hypertension disappear after removal of the renal tumor. In another patient, a 24-year-old girl, the hypertension was thought to be caused by polycystic kidneys, but subsequently the renal lesions were proved to be bilateral liposarcomas.[2a] No change in the blood pressure was elicited in the remaining six patients after nephrectomy.

TABLE 1.—*Atypical Chief Complaints and/or Findings in 183 Patients*

Symptom	Frequency
Weight loss	69
Pain (other than in the flank)	45
Fever	38
Weakness	37
Anorexia	24
Painless abdominal mass (only symptom)	12
"Prostatism"	10
Hypertension	8
Constipation	8
Vomiting	8
Cough	8
Varicocele	5
Dyspnea	5
Uremia	3
Miscellaneous*	15

*Includes edema of legs (3), papilledema (2), hemoptysis (2), chills (2), numbness of lower extremities (2), vertigo (1), sweating (1), anuria (1), impotentia (1).

Asymptomatic noncollapsible varicocele was present in five patients, and in each a large renal neoplasm was found. Of the three patients who had uremia, two had generalized amyloidosis and one nephrosclerosis. Of the 15 cases grouped under "miscellaneous," in about two-thirds the symptoms were due to the renal tumors or their metastases and in the remainder to other concomitant pathological conditions.

TABLE 2.—*Patients with Atypical Syndromes*

Symptoms	Patients, No.
1. Fever, weakness, anorexia, loss of weight	95
2. Pain, alone or with any of the above symptoms	31
3. Painless abdominal mass	12
4. Miscellaneous	45
Prostatism	10
Polycythemia	9*
Hypertension	6
"Lumps" in skin (3) and in skull (1)	4
Cholecystitis	3
Uremia: amyloidosis (1), polycystic kidneys (1), hypertension and nephrosclerosis (1)	3
Nephrolithiasis	2
Visual difficulties, hemangiomatosis (Lindau's disease)	2
Varicocele only	1
Aneurysm of abdominal aorta	1
Routine check-up (no symptoms)	7
Roentgenograph of chest	3
Intravenous urogram	3
"Barium" enema	1

*Four had hematuria.

Atypical Syndromes

Depending on the type of symptom-complex, the 183 patients were separated into four main groups (table 2).

Group 1.—Fever, weakness, anorexia, and loss of weight, usually in combination but at times independently, occurred in 95 (about 50%) of the 183 patients and in 16.5% of the entire group of 577 patients with renal cancer seen at this hospital. Incidentally, these symptoms and/or findings were often present in patients with hematuria, but, as stated in the introduction, those patients were excluded from this study.

It is difficult to explain the cause of fever in association with renal tumors. Hemorrhage, necrosis, and/or infection of the renal growth, extensive tissue destruction due to widespread metastases or to a metastasis to the heat regulatory center, and body reaction to "foreign" tumor protein absorption have been proposed as possible explanations for the rise in temperature. While it is true that any one of the foregoing may be present in some patients with renal neoplasms, in others none of the above-mentioned changes could be demonstrated. Furthermore, hyperpyrexia was present with about equal frequency in this series, irrespective of the pathological type of renal tumor, i. e., clear versus granular cell carcinomas. Thus, the histological make-up of the kidney parenchymal neoplasms was apparently not an important factor in the cause of fever. This observation is in disagreement with that reported recently by Bottiger and Ivemark.[8] These authors found that, of 38 patients with clear cells in the tumors, 17 (45%) had fever, while of 21 with granular cells in the specimens only 2 (10%) had fever. Anorexia, weakness, and loss of weight, with or without fever, were usually present in patients with demonstrable metastases. These patients also had elevated erythrocyte sedimentation rates.

Group 2.—There were 31 patients (17% of the 183 with "atypical" symptoms, or 5.4% of the 577 with renal tumors) in whom pain other than in the flank was the leading symptom. It usually occurred alone and at times in association with the symptom-complex described under group 1. Metastases, usually in bone, were present in these patients. The pain varied in location, radiation, and intensity and depended usually on the site and size of the metastasis. The pain was often refractory to the usual analgesics, but on recognition of its underlying cause the occult renal tumor was subsequently discovered.

Table 3.—*Site and Number of Demonstrable Metastases in Eighty Patients when Their Renal Tumors were Discovered**

Bones			55
Spine	13	Femur	4
"Multiple bones"	12	Scapula	4
Pelvic girdle	7	Skull	3
Ribs	5	Clavicle	2
Humerus	4	Carpal bones	1
Internal organs			52
Lungs	32	Thyroid	2
Brain	9	Opposite ureter	1
Liver	4	Adrenal	1
Opposite kidney	2	Duodenum	1
Lymph nodes and soft tissues			17
Superficial lymph nodes	5	Skin	2
Retroperitoneal lymph nodes	5	Vesicovaginal septum	1
Retroperitoneal tissue	3	Gums	1

*In about one-half of the cases the findings in the biopsy of the metastasis lead to investigation of the genitourinary tract and discovery of the renal tumor.

Group 3.—There were 12 patients (6.6% of the 183 with atypical symptoms, or 2% of the 577 with renal neoplasms) with a painless abdominal mass as their only complaint or incidental finding. The reasons for their inclusion under "atypical syndromes" have been discussed in the introduction and again under "Symptoms and Findings." Nevertheless, it should be emphasized once more that in most instances the painless mass was erroneously thought to be an enlarged spleen or liver rather than a kidney.

Group 4.—This group included 45 patients (24.4% of the 183 and 7.8% of the 577) who could be subdivided into the following categories: (*a*) patients whose symptoms and findings were due to a concomitant disease such as prostatism, polycythemia, hypertension, and cholecystitis; (*b*) patients who presented metastases to superficial lymph nodes, skin, etc.; (*c*) persons, free of symptoms, who reported to the hospital for a routine examination; and (*d*) rare cases in which the renal cancer was unsuspected clinically but was found incidentally at autopsy.

The therapeutic results in groups 3 and 4 (with the exception of those patients who came with metastases) were better than in groups 1 and 2.

Laboratory Findings

For the purpose of the present study only the reports of urinalysis, hemoglobin level determination, and erythrocyte sedimentation rate made on admission were reviewed.

The results of the urinalyses in the 183 patients regarding the presence or absence of microhematuria showed that in 109 patients, or 59.5%, there were no erythrocytes in the urine; in 56 patients only a "few" were found. In 14 patients there were "many" red blood cells, and in the remaining 4 patients, all of whom had polycythemia, the urine was "loaded" with erythrocytes. These were the only patients in the entire group who, despite gross hematuria, were included in the present study because of the unusual and interesting association of renal cancer and polycythemia. Incidentally, gross hematuria may occur in patients with polycythemia, without renal cancer.

The determination of the blood hemoglobin level was done in 181 patients. Anemia usually occurred in patients with large tumors and metastases and in those with the syndrome of fever, weakness, anorexia, and loss of weight. In none of the patients was the anemia due to tumor hemorrhage. In a few cases the anemia was severe (6.5 Gm. of hemoglobin). On the other hand, there were nine patients who suffered from polycythemia and renal tumor. These cases have been reported by Damon and associates[4] in 1958. Five of the patients came primarily because of the polycythemia, and the renal tumor was incidentally discovered during clinical evaluation. The remaining four were admitted because of gross hematuria; in these patients a renal neoplasm was found associated with polycythemia. Two of the nine patients were alive 15 and 4 years, respectively, after nephrectomy without evidence of tumor recurrence or metastases and with normal red blood cell counts.

The erythrocyte sedimentation rate was recorded in 97 patients. It was found elevated, from 35 to 140 mm. in one hour (Westergren method), in 73 patients and normal in 24. Of those patients who had an elevated erythrocyte sedimentation rate 53 (72.6%) are dead, while only 2 are alive (2.7%); 18 could not be traced. Of the 24 patients with normal erythrocyte sedimentation rate, 15 are dead, 5 (20.8%) are alive, and 4 could not be traced.

Patients with anemia tended to have a high sedimentation rate. The "slowest" sedimentation rates, below normal, were obtained in patients with polycythemia. An elevated erythrocyte sedimentation rate was usually found in those patients who had large tumors and/or metastases and who subsequently died of the disease. Hyperfibrinogenemia and increase in plasma of alpha-2 globulin has been reported[8] recently as being present in patients with elevated erythrocyte sedimentation rate and with renal tumor. In none of the cases in our series were the plasma fibrinogen and alpha-2 globulin levels determined.

Metastases

There were 80 patients of the 183 in whom demonstrable metastases were present when the renal tumors were discovered. The location and number of metastases are shown in table 3.

Though the total number of metastases in this group was larger in the skeletal system (43 times) than in any of the internal organs, lymph nodes, or soft tissues, the lungs were the organs most commonly affected (32 patients). Metastases to bones tended to be multiple. The spine was most frequently involved (13 times). Severe low back pain radiating to the abdomen was usually present in patients with metastases to the lumbar spine. Sciatic pain characterized metastatic involvement of the sacroiliac joint. So-called pathological fractures usually occurred when the shaft of the humerus or femur was the site of metastases. Metastases to the lungs were usually silent, though in some instances the patients complained of fever and loss of weight, and a few had dyspnea, fatigue, and hemoptysis.

The nine patients with brain metastases were admitted to the Neurological Institute because of symptoms and findings characteristic of a cerebral expanding lesion. In some of these cases a diagnosis of a primary brain tumor was made, and in two the "metastatic tumor" was surgically removed. After microscopic studies the silent renal tumor was discovered.

One patient, a 54-year-old woman, underwent several operations to remove a primary carcinoma of the thyroid and subsequently some of its metastases. A partial ureterectomy on the right was performed because of supposed ureteral metastasis from the thyroid carcinoma. About three years after the first operation, hematuria occurred. It was then discovered that the primary lesion was a slow-growing carcinoma of the left kidney, which had spread diffusely, with metastases to the thyroid and right ureter and later also to the right adrenal gland and right kidney (fig. 1).

Involvement of the superficial lymph nodes occurred as a rule in the more advanced or disseminated stage of renal cancer. Retroperitoneal tissues and lymph node involvement were found in eight cases. It is probable that this complication was more common but was not demonstrated because many patients were not subjected to nephrectomy. Skin metastasis as the initial symptom was present in two patients. In one the metastasis was a "hot pulsating" mass in the occiput[9]; in the other the metastasis resembled a verruca vulgaris but with an indurated base. Incidentally, pulsating metastasis from a renal neoplasm has long been recognized.[10] Metastasis from a silent clear-cell carcinoma of the kidney to the vesicovaginal septum was found in a 40-year-old woman who came because of dysuria.

In several patients with so-called solitary metastasis excision of the metastasis as well as the renal tumor was carried out. None of these patients was cured, and all eventually died of multiple metastases. One patient, a 71-year-old man, complained of pain in his right knee. A roentgenogram showed an osteolytic lesion; a bilateral retrograde pyelogram showed positive findings in the right kidney (fig. 2). The microscopic diagnosis was clear-cell carcinoma of the kidney, with a pattern identical to that of the osseous lesion. A roentgenogram of the chest, obtained 10 months after nephrectomy, and amputation of the right lower extremity revealed extensive pulmonary metastases.

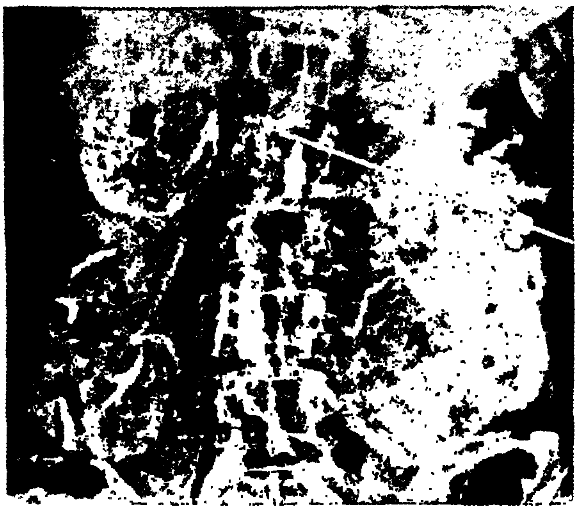

Fig. 1.—Translumbar aortogram obtained three years after radical thyroidectomy for primary carcinoma of thyroid. Note, *A*, tremendous enlargement of lower half of left kidney and extensive pooling of contrast medium; *B*, enlargement of right adrenal gland, also with pooling; *C*, probable metastasis to right kidney in hilar area; and, *D*, shadow of metallic stitches along course of right ureter from previous ureteral surgery.

Such was the outcome in the other group of patients seen at this hospital with renal neoplasms but with the classic urologic symptom-triad and who also had removal of their "solitary" metastasis. Several reports have appeared in the medical literature, however, of patients who apparently were "cured" after excision of primary lesion and of the metastasis.[11] Among the 183 patients there were 2 in whom a solitary pulmonary "metastasis" was found along with a renal tumor. Nephrectomy and subsequently lobectomy were carried out. The renal lesion was found on pathological examination to be a primary carcinoma of the kidney; but the pulmonary "metastasis" turned out to be, in each instance, a hamartoma of the lung. Both patients are alive and well.

Summary

A detailed clinicopathological analysis of the records of 577 patients with renal tumor from the Squier Urological Clinic and Presbyterian Hospital revealed that in 183 patients, or 31.7%, the classic symptom triad of gross hematuria, pain in the flank, and flank mass was absent. These patients, on the other hand, sought medical advice for the relief of nonurologic or "atypical" symptoms or signs. In 138 patients, i. e., in 75% of the 183 and 24% of the 577 with renal tumors, one or usually several of the following complaints or findings were recorded: loss of weight, pain other than in flank, cryptic fever, unexplained weakness, and painless abdominal mass. In the remaining 45 patients, i. e., in 25% of the 183 and 7.8% of the 577 with renal neoplasms, the renal tumor was "silent" and was discovered incidentally during clinical evaluation for "prostatism," hypertension, polycythemia, nephrolithiasis, etc., or at autopsy.

Gross hematuria was absent in 179 patients (the remaining 4 had polycythemia and did complain of gross hematuria). In 109 (59.5%) of these patients microscopic examination of the urine failed to reveal any erythrocytes. In 56 patients the urinalysis showed a "few" red blood cells and in 14 "many." The urine was "loaded" with red blood cells in four. Thus, significant microhematuria in this group was present in only 18 patients or 10% (including those with polycythemia).

Demonstrable metastases were already present in 80 of the 183 patients (40%) when the renal tumor was discovered. Metastases involved the skeletal system with almost equal frequency as the internal organs, including the soft tissues. The lungs, however, were the most commonly involved organs. In no instance was there a cure achieved whenever a so-called solitary metastasis was found and excised prior to or after nephrectomy.

A high erythrocyte sedimentation rate was usually observed in patients who came with or without demonstrable metastases but who subsequently died of the renal tumor.

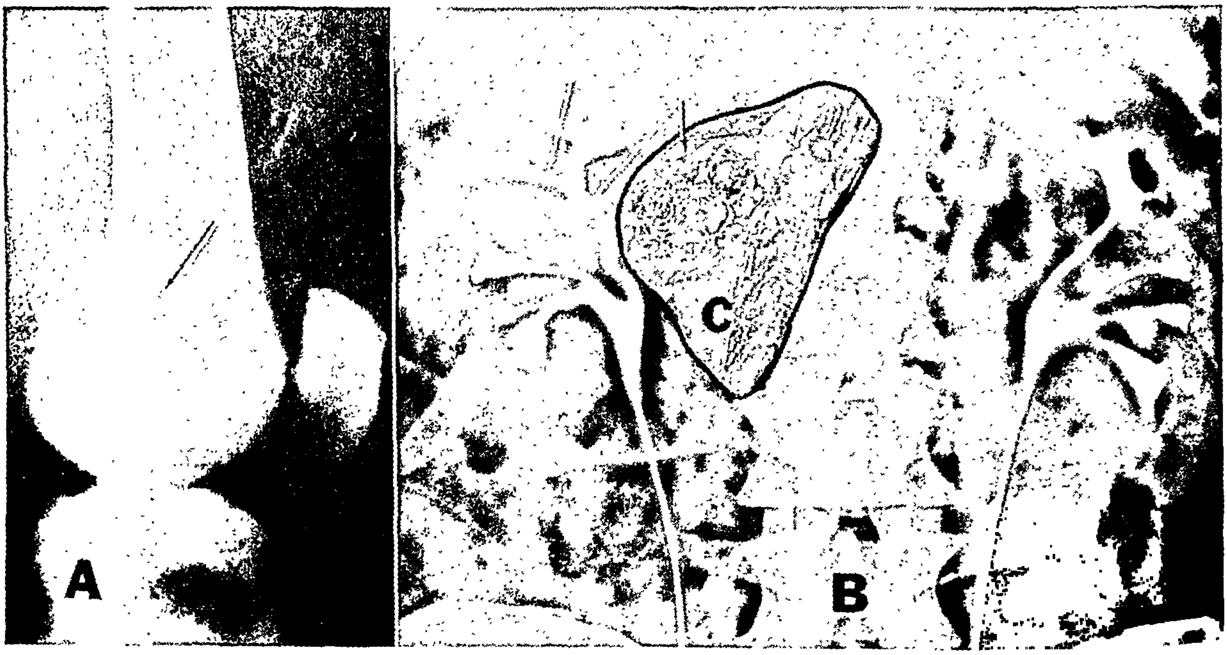

Fig. 2.—*A*, osteolytic lesión in condyle of right femur. Biopsy of lesion revealed that it was metastasis from clear-cell carcinoma of kidney. *B*, bilateral retrograde pyelogram showing curving of uppermost major calyx of right kidney. *C*, open renal specimen disclosing relatively small tumor (about 5 cm. in diameter) along periphery of midrenal segment.

About one-third of patients with renal cancer seen at this hospital had "atypical" or nonurologic symptoms. Because of this, a considerable period of time elapsed and a delayed rather than an early diagnosis was made. It is hoped that awareness of the significance and recognition of these atypical syndromes and of the value of the intravenous urography as an important diagnostic aid will bring about more instances of correct diagnosis at an earlier stage of this disease and thereby improve the present poor end-results.

620 W. 168th St. (Dr. Uson).

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DUODENAL DIVERTICULITIS WITH PERFORATION

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and
Lieut. Buell C. Cole, (MC), U. S. N.

A 52-year-old man was suddenly seized with severe pain in the epigastrium and the right upper quadrant of the abdomen. Vomiting began an hour later, but there was no hematemesis. At laparotomy the only abnormality found was a small round duodenal diverticulum which had perforated. About 1 cm. of the diverticulum was excised, and the remaining part was closed with inverting sutures. Recovery was uneventful. There have been 10 previous reports in English of similar cases of perforated duodenal diverticula.

Ten cases of perforated duodenal diverticula have been reported in the English-language literature. We wish to present an additional case of this unusual form of intra-abdominal catastrophe. The true incidence of duodenal diverticula remains unknown. Published figures vary from 0.8%, as reported by Glasier and Corbett,[1] to 5.76%, reported by Chitambar,[2] these figures being based on x-ray (gastrointestinal) examinations. Figures for the incidence of duodenal diverticula based on autopsy studies vary from 5.0%, reported by Horton and Mueller,[3] to 22.0%, reported by Ackermann.[4] There appears to be no definite sex predominance, and, while diverticula have been reported in all age groups, most are seen in patients in the 5th or 6th decades of life.

If one divides the duodenum into its usual three portions, diverticula have been reported in each. However, the incidence varies, with about 65% being located in the second portion, 25% in the third portion, and 5% in the proximal or first portion. Chitambar[2] in his series found that all patients with diverticula of the first portion of the duodenum had a history of duodenal ulcer perforation. These diverticula may appear on either the anterior or the posterior aspect of the duodenum, while diverticula of the second and third portions, unassociated with peptic ulcer disease, almost invariably appear posteriorly and medially.

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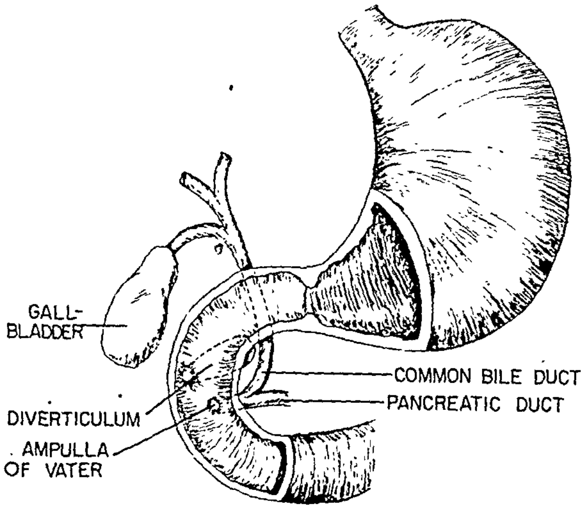
Signs, Symptoms, Diagnosis, and Treatment

The true origin of duodenal diverticula remains controversial. The three most prominent factors appear to be a weakening of the duodenal wall, an increase in the intraluminal pressure, and traction on the duodenal wall from without. The fact that most diverticula occur on the concave (mesenteric) border of the duodenum gives rise to the thought that the weakness is associated with the entrance of blood vessels, bile ducts, and pancreatic structures (see figure). The posteromedial wall of the duodenum contains more fat, which occasionally invades to the level of the submucosa; it is thought that this fat may produce a weakness or defect in the muscle layer.

Chitambar[2] reported that 31% of his patients had diverticula in other portions of the gastrointestinal tract and 13.8% had diverticula in portions of the small intestine other than the duodenum. Duodenal diverticula have no characteristic contours. The size may vary from 2 mm. to several centimeters in diameter, while the shape may be round, oval, bilobular, or mushroom-like. Multiple diverticula have been reported. Symptoms may be caused by dilatation of the diverticulum or by pressure on surrounding organs. Prominent symptoms include constipation, pain, belching, nausea and vomiting, and weight loss. There is no characteristic symptom complex, and diagnosis is largely by exclusion of other disease processes which might cause such attacks. The differential diagnosis may include ulcer disease, gallbladder syndrome, and pancreatitis. The presenting diagnosis of duodenal diverticula depends on demonstration of the lesion during gastrointestinal series with the aid of barium. Even then, one must remember that most patients with duodenal diverticula are asymptomatic and other disease processes must be ruled out.



Second-portion type of duodenal diverticulum.

Soon after recognition of duodenal diverticulosis as a definite entity, surgery was deemed imperative in every case. There was then a swing to the other extreme—all diverticula of the duodenum were looked on as inconsequential. It is now believed that most diverticula are symptomless and should be treated medically, if at all. However, there is a small, definite percentage of patients in whom diverticula are the source of symptoms, and it is in these patients that surgery should be contemplated. This figure has been estimated at 5% (pertaining only to patients with proved duodenal diverticula). Complications include acute inflammation, with the possible association of duodenitis, cholangitis, or pancreatitis, with the possibility of adhesion or fistula formation, or both. Hemorrhage is unusual but has been reported. Calculi, both primary and secondary from the biliary tree, have been found. Neoplasms have been recorded and obstruction has been described, including that of the duodenum itself, the pancreatic duct, and the biliary ducts. The most startling complication is that of perforation in a patient who had previously been asymptomatic.

Surgery is indicated in patients whose symptoms have been definitely attributed to the presence of a duodenal diverticulum and for most of the complications caused by duodenal diverticula. First-portion diverticula are approached surgically with much less difficulty than those in the lower portions. In a patient with the history of peptic ulcer disease, subtotal gastrectomy is occasionally recommended as definitive treatment for diverticula of the first portion. In the absence of active ulcer disease this may be extravagant. Small diverticula may be safely inverted, but the better procedure is to excise them about 3 or 4 mm. distal to the duodenal wall and carefully to close the resultant defect. Diverticula of the second portion of the duodenum are technically difficult to manage and, frequently, are even difficult to find. Complete mobilization of the duodenum by the Kocher operation is essential. Other maneuvers, such as distending the duodenum with air or inserting a finger into the duodenal diverticulum through an anterior wall duodenotomy, may be required. Special care is demanded in treating patients with those diverticula which originate immediately adjacent to the ampulla of Vater. A choledochotomy with a probe threaded down the common duct and through the ampulla of Vater may be of vital aid. A diverticulum around the ampulla of Vater is best treated by excising the majority of the sac and inverting the remaining neck with a two-layer closure. Diverticula of the third portion of the duodenum may present a tedious technical problem. The approach is through the transverse mesocolon and occasionally Treitz's muscle must be divided.

Perforation of a duodenal diverticulum is rare. Of the 10 cases previously reported in the English literature, only one was diagnosed preoperatively while 3 were diagnosed at autopsy in spite of previous laparotomies. The mortality of the previously reported cases is 30%, all deaths being due to failure of recognition of the disease process at the time of laparotomy. All patients in whom the diagnosis was made at the time of laparotomy survived.

Report of a Case

On March 7, 1959, a 52-year-old man was admitted to the surgical service of the U. S. Naval Hospital, San Diego, Calif., with a history of sudden, severe, epigastric and right upper quadrant abdominal pain about 17 hours prior to admission. The pain caused him to double over and he felt as if something were rapidly expanding in the upper portion of his abdomen. The pain remained constant and localized to the epigastrium and right upper quadrant. One hour later he vomited; there was no hematemesis. The pain, nausea, and vomiting persisted and he was brought to San Diego from an isolated outpost in the Arizona desert. He had had a normal bowel movement the day prior to his illness and there was no recent history of gastrointestinal or urologic symptoms. A duodenal ulcer had been demonstrated roentgenographically six years previously, but the patient had been asymptomatic for five years. There was no history of alcoholism or of intolerance to fatty foods, and he had never been jaundiced.

On examination the patient complained of upper abdominal pain which was less severe than it had been previously. His temperature was 101.2 F (38.4 C), pulse 88 beats per minute, and blood pressure 110/64 mm. Hg. Questionable dulness was present over the right lower lung field posteriorly, but pertinent findings were limited to the abdomen, where there was involuntary muscle guarding of the right side associated with marked tenderness in the right upper quadrant and moderate tenderness in the right lower quadrant. There was localized rebound tenderness over both the right upper and the right lower quadrants but no referred rebound tenderness. No organs or masses were palpable. The intestinal sounds were hypoactive to absent, and there was marked tenderness to percussion over the right flank. Laboratory studies revealed a leukocyte count of 17,300 per cubic millimeter, with 84% neutrophils, hematocrit value of 43%, a normal urinalysis, and a serum amylase level of 120 units. A repeat white blood cell count was reported as 22,600 per cubic millimeter, with a shift to the left. Acute abdominal x-ray series revealed only gas in the splenic flexure of the colon and an obscured right-sided psoas shadow. Possibilities for differential diagnosis included a perforated duodenal ulcer, acute cholecystitis, and acute retrocecal appendicitis. Immediate laparotomy was recommended.

Surgery, with the patient under general endotracheal anesthesia, revealed a minimal amount of serous fluid in the peritoneal cavity, associated with a normal gallbladder and normal appendix. The duodenum at first appeared normal, but moderate edema of the surrounding tissues was noted. A small area of frothy white discoloration was seen posteriorly through the peritoneum medial to the first portion of the duodenum and overlying the superior aspect of the head of the pancreas. The duodenum was mobilized by the Kocher technique and the retroduodenal tissues were found to be markedly edematous, although no pus or fluid was encountered. With the duodenum reflected medially a small nubbin of mucosa was seen, and closer inspection revealed this to be a small diverticulum, the tip of which had necrosed and sloughed. The diverticulum was round, about 1.5 cm. in remaining length, and admitted the little finger snugly. It ran tangentially downward in the posteromedial wall of the second portion of the duodenum and, after an anterior wall duodenotomy had been made, was found to enter the duodenum immediately adjacent to the ampulla of Vater. About 1.0 cm. of the diverticulum was excised and the remaining portion was closed with two layers of interrupted, inverting 000 black silk sutures. A gastrostomy tube was placed for postoperative drainage and decompression and the duodenotomy closed with a single layer of inverting 000 black silk sutures. The paraduodenal area was drained with a large Penrose drain brought out through a separate stab wound in the upper quadrant.

The patient's postoperative course was uneventful and an ulcer-type diet was initiated on the third postoperative day. The sutures were removed on the seventh day, the Penrose drain on the eighth day, and the gastrostomy tube on the ninth postoperative day, at which time the patient was asymptomatic and fully ambulant. Microscopic examination of the specimen revealed duodenal mucosa, submucosa, and normal muscle layers, with ulceration and perforation. The edematous tissues surrounding the perforation showed hemorrhage with both acute and chronic inflammatory cells. A barium "meal," two weeks after surgery, revealed minimal scarring of the duodenum, with no active ulceration and no evidence of a diverticulum.

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CLINICAL NOTES

ISCHEMIC NECROSIS DUE TO ADMINISTRATION OF METARAMINOL

REPORT OF A CASE

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The use of sympathomimetic amines, such as arterenol (Levophed) bitartrate and metaraminol (Aramine) bitartrate, as vasopressor agents in the treatment of clinical hypotension has received widespread acceptance. The occurrence of ischemic necrosis secondary to the administration of arterenol has been well documented.[1] Due to the physiological similarity of these drugs it could be expected that such a complication would arise with extensive use of metaraminol. One such case was reported recently.[2] The following is a report of a similar case.

A 62-year-old man was admitted to the Latter-day Saints Hospital on April 17, 1959, with the type of electrocardiographic changes found in patients with acute, posterior myocardial infarction, a white blood cell count of 11,200 per cubic millimeter, and a serum transaminase level of 56 Todd units. At the time of admission the patient's blood pressure was 130/100 mm. Hg in both arms, and his pulse rate was 60 per minute and regular. On the third hospital day the patient suddenly became unresponsive. Neither respirations, pulse, nor blood pressure could be obtained. Artificial respiration was instituted, after which the patient began Cheyne-Stokes respirations. He was given, intravenously, 2 cc. of methoxamine (Vasoxyl) hydrochloride and 2 cc. of nikethamide (Coramine). An intravenous infusion of 50 mg. of metaraminol diluted with 5% dextrose in 1,000 cc. of water was started in the right antecubital vein. The heart sounds once more were audible, but were noted to be irregular. An electrocardiogram showed varying degrees of atrioventricular block, with a ventricular rate of 60 per minute.

The intravenous infusion infiltrated after 16 hours, and a cut-down was done in the right greater saphenous vein. Since, because of vasospasm, a polyethylene catheter could not be inserted, an 18-gauge needle was tied in and left in place. Because of the appearance of bilateral basilar rales the patient was digitalized with 1.2 mg. of intravenously given lanatoside C (Cedilanid) over a 6-hour period. The infusion dose of metaraminol was increased to 100 mg. diluted with 5% dextrose in 1,000 cc. of sterile water and given at a rate of 30 drops per minute. On the fifth hospital day the patient's blood pressure was 90/60 mm. Hg and the pulse rate 44 per minute, with a 2:1 atrioventricular block. There was noted to be an area of discoloration extending proximally from the site of the cut-down. This was about 11 by 8 cm., with a bluish discoloration of the edges and central blanching. There were three bullous, vesicular lesions varying from 1 to 2.5 cm. in diameter. The cut-down was discontinued, restarted in the left leg, and continued until the patient's death. The site was then infiltrated with 5 mg. of phentolamine (Regitine) hydrochloride in 20 cc. of distilled sterile water; however no change was noted. The infiltrated right antecubital fossa remained normal. On the eighth hospital day the patient died. At this time it was noted that the vesicles had ruptured and the underlying tissue was bluish in color and appeared gangrenous.

Comment

Bryant and Howard,[3] in experiments on dogs, could not produce tissue sloughs by intravenous and subcutaneous administration of metaraminol. Only one case of rubor and ecchymosis developed, but it subsided over a three-day period. However, tissue sloughs were readily produced by slow, subcutaneous infusions of levarterenol. On this basis, these authors concluded that metaraminol could be given by intravenous infusion without the danger that inadvertent extravasation would lead to extensive soft tissue sloughs. Stechel and associates[4] have reported no thrombophlebitis or tissue sloughs in 42 patients studied; however, soft tissue necrosis occurred in the patient here reported, concomitant with the administration of metaraminol.

The use of phentolamine[5] and piperoxan hydrochloride[6] in the treatment of such complications has met with beneficial results in some cases. The lack of response in the patient under discussion probably was due to the lapse of time between the onset of tissue changes and treatment.

Dr. David E. Smith Jr. gave permission for the report of this interesting case, and Drs. S. J. Altman and Ernest Wilkinson gave helpful suggestions.

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FATAL THROMBOCYTOPENIC PURPURA AFTER ADMINISTRATION OF SULFAMETHOXYPYRIDAZINE

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Sulfamethoxypyridazine (kynex; also available as Midicel) has been available to members of the medical profession for more than two years. During that period an estimated 4 million prescriptions have been dispensed for this drug in the United States.[1] It has acquired an enviable reputation for safety, efficacy, and ease of administration; it has a range of therapeutic effectiveness comparable to that of sulfadiazine.[2] It has a distinct advantage over the older sulfonamides in that effective blood levels can be maintained in a patient with a single daily dose.[3]

Minor adverse effects occurring after therapy with sulfamethoxypyridazine include headache, anorexia, rash, fever, arthralgia, sore throat, "giddiness," and "shivering."[4] Of the more serious adverse effects thrombocytopenia has been reported in two instances; leukopenia, hemolytic anemia, and focal hepatitis each has been reported once.[5]

Four fatalities have been reported after sulfamethoxypyridazine administration, one from aplastic anemia[6] and three from "hypersensitivity myocarditis."[7] In one of the latter fatalities the myocardial changes were thought to be only a contributing factor, while in two they were assumed to be the direct cause of death. The present report deals with fatal thrombocytopenic purpura occurring after administration of sulfamethoxypyridazine.

Report of a Case

The patient, a 34-year-old man, was first examined on March 20, 1959, because of a suprapubic burning sensation of 10 days' duration. The patient's history was noncontributory except for an episode of urinary frequency and hematuria five years earlier which had been treated with a "sulfa" drug. There was no history of drug allergy, and he had received no medicaments in the recent past.

Physical examination revealed tenderness and swelling of the right lobe of the prostate. Prostatic massage was not done because the patient complained of exquisite tenderness; consequently, prostatic secretion was not obtained for microscopic examination. Urinalysis revealed no glucose or protein and no microscopic abnormalities. Sulfamethoxypyridazine was prescribed in an initial dose of 1.0 Gm., to be followed by 0.5 Gm., daily. Additional therapy included local heat in the form of hot tub baths.

At the end of one week he was asymptomatic and the prostate was no longer tender. On the 10th day of therapy with sulfamethoxypyridazine he developed an erythematous rash of both legs and noted some bleeding from the gums. On the 11th day he was admitted to Saint Luke's Hospital because of right flank pain and gross hematuria.

Physical examination revealed a blood pressure of 140/90 mm. Hg, pulse rate of 68 per minute, and temperature of 37.8 C (100 F). There were multiple petechiae on both legs, which in some areas seemed to coalesce (fig. 1). There were lesser numbers of petechiae on the abdomen, chest, and arms. Several hemorrhagic bullae were present within the buccal cavity (fig. 2). The heart showed a regular sinus rhythm with no murmurs. The lungs were clear to percussion and auscultation. The liver and spleen were not palpable, and there was no lymphadenopathy. Rectal examination was noncontributory, and the stool was normal in color. Neurological examination was normal. The patient was alert and cooperative.

The admission laboratory examinations revealed a hemoglobin concentration of 12.9 Gm.%; hematocrit value, 39%; white blood cell count, 9,300 per cubic millimeter, with 74% segmented neutrophils, 8% band cells, 15% lymphocytes, and 3% monocytes. The sedimentation rate (Wintrobe) was 4 mm. per

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From the Department of Medicine, Saint Luke's Hospital.

hour. The platelet count was 112,000 per cubic millimeter. The bleeding time was seven minutes and 30 seconds; clotting time, eight minutes (Lee-White method); and there was no clot retraction at the end of 24 hours. Plasma fibrinogen value was 0.41 Gm. per 100 cc. Prothrombin time (Quick) was 26% but rose to 52% after administration of 50 mg. of phytonadione (Mephyton), a preparation of vitamin K. The urine showed a specific gravity of 1.028 with a pH of 6.0, urine protein was 4+, and result of the test for glucose was negative. The urine was grossly bloody and did not contain porphyrins.

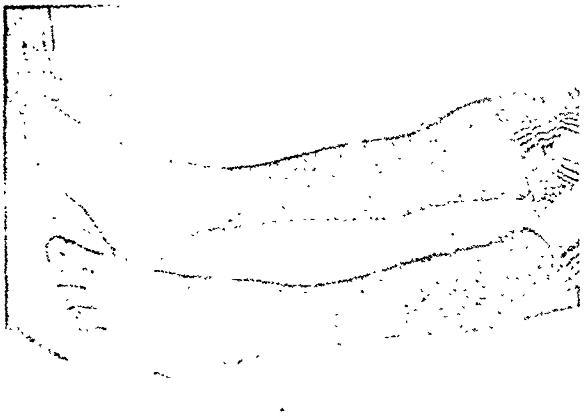

Fig. 1.—Multiple petechiae on legs.

The blood sugar level was 134 mg. per 100 cc.; nonprotein nitrogen content, 35 mg. per 100 cc.; carbon dioxide—combining power, 28 mM. per liter; serum sodium content, 135 mEq. per liter; serum potassium content, 4.3 mEq. per liter; plasma chlorides content, 100 mEq. per liter; serum calcium level, 11.8 mg. per 100 cc.; phosphorus level, 2.7 mg. per 100 cc.; and total protein content, 9.2 Gm. per 100 cc. The free serum sulfonamide level was 4.3 mg. per 100 cc.

The patient remained alert and cooperative throughout the first hospital day. The bleeding from the gums decreased, although the urine remained grossly bloody. On the morning of the second hospital day the platelet count was 18,000 per cubic millimeter. The patient appeared lethargic, complained of headache, and experienced two emeses of coffee-ground vomit which were projectile in nature. By noon of the second hospital day he was comatose and responded only to painful stimuli. A lumbar puncture was performed, and the fluid obtained was grossly bloody. The spinal fluid cell count was 750 white blood cells and 1,169,250 red blood cells per cubic millimeter. A marrow biopsy revealed large numbers of megakaryocytes, with no evidence of "pseudopodia" (fig. 3).

Initially he received 40 units of ACTH and 1.5 mg. of dexamethasone (Decadron, Deronil). On the first hospital day he received 90 mg. of prednisone by mouth in three divided doses and 100 mg. of hydrocortisone sodium succinate (Solu-Cortef) intravenously. On the second hospital day he received 100 mg. of prednisolone intravenously every four hours. Two units of fresh whole blood were administered, followed by 250 cc. of platelet-rich plasma every four hours until a total of 1,750 cc. had been given. After the last 250 cc. of plasma the platelet count was 16,000 per cubic millimeter.

On the third hospital day his respirations became labored and the patient was cyanotic. A tracheotomy was performed and positive pressure was employed. He died on the third hospital day. Permission to perform an autopsy was not granted.

Comment

It seems reasonable to assume that the thrombocytopenic purpura which developed in this patient was a result of his sensitivity to sulfamethoxypyridazine. In all of the previously recorded instances of a hematological disorder occurring after administration of this drug, the patients reported had received at least 1 Gm. per day. The case of this patient, who received only 0.5 Gm. per day, serves to emphasize that in a sensitized person severe toxic manifestations may occur irrespective of the dose. The serum sulfonamide level of 4.3 mg. precludes the possibility of an excessive accumulation in the patient's blood.

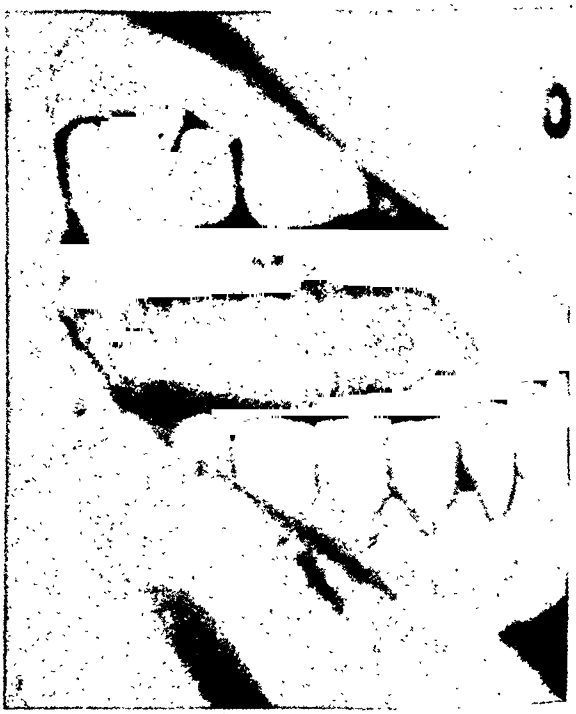

Fig. 2.—Hemorrhagic bullae within buccal cavity.

The administration of many drugs may be complicated by petechial purpura. In some instances the purpura is thought to be caused by a vascular or angiotoxic factor, while in others definite thrombocytopenia is present. The thrombocytopenia may be due either to a direct toxic effect on the marrow or to an immunological type of response in which the platelets are destroyed and the megakaryocytes are inhibited from forming and delivering platelets.[8] Because of the adequate numbers of megakaryocytes, with no pseudopodia, in the marrow of this patient, it seems likely that this was an immunological type of response rather than a toxic effect. That an element of angiotoxic or vascular damage existed also seems probable.

Lehr,[9] in a review of sulfonamide toxicity, concluded that, while the over-all incidence of toxic reactions has declined to a remarkable degree with the advent of the newer sulfonamides, the type and character of the toxic reactions has not changed materially.

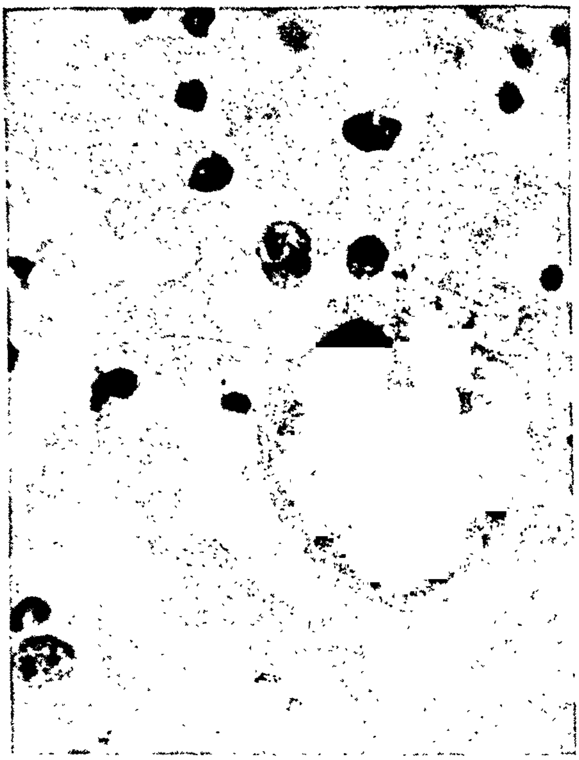

Fig. 3.—Marrow biopsy specimen, showing megakaryocyte, with no "pseudopodia."

The blood dyscrasias have always formed a small percentage of the toxic reactions from sulfonamides. Thrombocytopenia is said to occur in less than 0.3% of cases, but the mortality from this particular complication is high.[10]

In reviews [11] of the over-all incidence of serious toxic reactions from sulfonamides, sulfathiazole led the list with 18.6% and sulfapyridine was second with 15.9%, followed in order by sulfanilamide, 11.9%; sulfamerazine, 9.5%; sulfadiazine, 6.5%; sulfisoxazole, 2.8% to 8.8%; and sulfamethazine, 6%.

Jackson [12] recently estimated the incidence of adverse reactions from sulfamethoxypyridazine at 6%. Most of these reactions have not been of a serious nature and have responded to withdrawal of the drug. In an attempt to assess the toxicity of this drug, a series of 110 patients was given a dose three times greater than that recommended by the manufacturers.[4a] Of these patients 10% showed mild subjective symptoms, but there were no serious manifestations of drug sensitivity or toxicity.

Summary

A fatal case of thrombocytopenic purpura followed the administration of sulfamethoxypyridazine. A review of the current literature would seem to indicate that this drug has established a record for safety comparable, and in some respects superior, to the earlier sulfonamide preparations. Despite this, four deaths have been attributed to the drug within the past two years and all of the adverse reactions (except crystalluria) reported with the older sulfonamides have also been reported with this drug. Although the incidence of adverse reactions may be somewhat lower with the newer sulfonamides, they must be administered with the same respect that is accorded the older preparations.

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REVERSIBLE MANIFESTATION OF THYROIDITIS

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The problem of diagnosis and treatment of the thyroid nodule is a vexing one and has been the subject of many communications. I have recently had an instructive experience with a solitary thyroid nodule which proved amenable to medical treatment.

A 40-year-old housewife, the mother of five living children, was referred to me because of acute onset of swelling of the anterior part of the neck. A few days previously she had noted pain in the left side of her neck which was aggravated by dorsiflexion of the neck. A tender swelling in the left, anterior part of the neck was noted the day before examination. The only recent illness the patient had had was an upper respiratory infection accompanied by rhinorrhea and sore throat, two weeks previously, from which she obtained symptomatic relief by taking several doses of aspirin. Fever had not been noted. The only previous history at all suggestive of thyroid disorder was a bout of tachycardia two years previously during a pregnancy which resulted in a stillbirth.

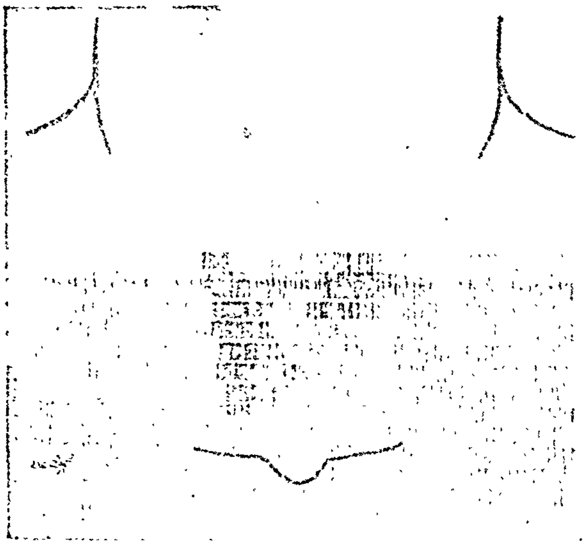

Fig. 1.—Scintiscan (12/23/58): scanning dose 100 μc, 24-hr. I^{131} uptake 38%.

Examination revealed an oral temperature of 100 F (37.8 C), a regular pulse rate of 100 per minute, and a blood pressure of 140/88 mm. Hg. Findings of a general physical examination were normal except for enlargement, tenderness, firmness, and warmth of the left lobe of the thyroid. The right lobe felt normal in size, consistency, and configuration.

Laboratory tests revealed the serum protein-bound iodine level to be 6.8 mcg.%, the 24-hour radiodine (I^{131}) uptake 38%, and the erythrocyte sedimentation rate (Wintrobe) 5 mm. per hour. The hemoglobin level was 10 Gm.%, the hematocrit 32%, and the white blood cell count 10,500 per cubic millimeter, with 75% polymorphonuclear leukocytes, 24% lymphocytes, and 1% monocytes. A scintiscan of the thyroid region with use of 100 μc of radioiodine (I^{131}), revealed failure of uptake over a large area of the lower portion of the left lobe (fig. 1).

A diagnosis of subacute thyroiditis was made and treatment instituted with sodium levothyroxine, 0.2 mg. daily, and prednisolone, 5 mg. three times daily. This was continued for three weeks, during which time the left lobe of the thyroid receded in size. The dosage of prednisolone was reduced to 5 mg. twice daily, and complete disappearance of the enlargement was noted after four more weeks. Three weeks later, after a total time of 10 weeks, therapy with prednisolone was discontinued; administration of thyroxin was stopped three weeks later. Concurrently the patient had been given doses of iron orally, and her blood cell count had reverted to normal. Except for transient palpitation one month later, she felt well and noted no recurrence of the thyroid swelling.

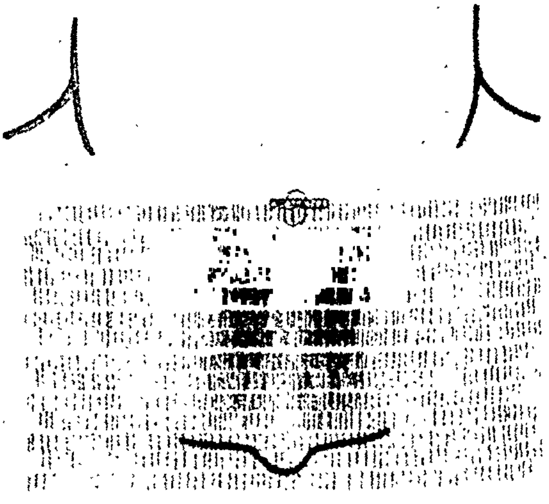

Fig. 2.—Scintiscan (7/9/59): scanning dose 92 μc, 24-hr. I^{131} uptake 29%.

Six and one-half months after first being seen, she continued to feel well. Laboratory tests at that time revealed the following findings: blood protein-bound iodine level of 6.9 mcg.%; 24-hour radioiodine (I^{131}) uptake of 29%; and blood cell count showing a hemoglobin level of 14 Gm.%, a hematocrit of 42%, and a white blood cell count of 6,400 per cubic millimeter, with 66% polymorphonuclear leukocytes, 30% lymphocytes, 1% basophils, 2%

monocytes, and 1% eosinophils. A scintiscan made 24 hours after administration of 92 μc. of radioiodine (I^{131}) revealed a normal distribution of iodine throughout the thyroid gland (fig. 2).

This report has been presented because it affords an unusual opportunity to demonstrate recovery of radioiodine (I^{131}) uptake by a portion of the thyroid gland after subacute inflammation. It also demonstrates the efficacy of short-term corticosteroid and thyroxin therapy in the management of this condition.

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ANAPHYLACTIC REACTION TO CHYMOTRYPSIN

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and
Henry Ritter Jr., M.D., Redwood City, Calif.

Proteolytic enzyme therapy has been employed in various diseases in which its anti-inflammatory and fibrinolytic effects have been of value. Among such agents, aqueous chymotrypsin (Chymar) has been described as relatively free of undesirable side-effects.

In the brochure [1] accompanying this product it is stated that, "Although sensitivity to chymotrypsin is uncommon, the usual precautions should be exercised in those patients with known allergies or sensitivities."

The toxicology of both crystalline trypsin and chymotrypsin has been studied by Hendley and associates [2] in extensive animal experiments. Large doses of chymotrypsin administered intravenously resulted in marked lowering of blood pressure and irreversible shock with respiratory arrest and cardiac standstill. Vascular collapse was not a uniform phenomenon but was dependent on species sensitivity. Generalized hemorrhagic diathesis involving lungs, myocardium, intestine, kidneys, and liver was also produced. Chymotrypsin in large doses was found to be a potent anticoagulant. Death in some of these animals, however, could not be attributed to massive hemorrhage but was believed to be due to a direct toxic effect on the central nervous system. Guzzon [3] compared the "anaphylactic power" of trypsin and chymotrypsin and their precursors. He, as well as Hendley, concluded that chymotrypsin was less toxic than trypsin and was far better tolerated in their animal studies.

Hypersensitivity to both trypsin and chymotrypsin has been well documented in human beings by Fullgrabe [4] and Lichtman. [5] They concluded that the sesame oil carrier, rather than the enzymes, was responsible for the allergic reaction.

It is therefore considered worthwhile to report the following case, since neither trypsin nor sesame oil carrier could be implicated. We have been unable to find any reference in the medical literature to the reaction which we are about to describe.

Report of a Case

A 44-year-old man was treated by one of us (H. R.) for acute epididymitis, as an office patient. He received 10 consecutive daily injections of aqueous chymotrypsin, 1 cc. each, intramuscularly, into the buttocks, in conjunction with antibiotic therapy. Due to recurrence of the epididymitis on his return to work, this man was hospitalized for 13 days, receiving 1-cc. injections of aqueous chymotrypsin twice daily for 3 days. Five days after hospital discharge residual epididymal swelling was still noted, so a 17th 1-cc. injection of aqueous chymotrypsin was administered intramuscularly. Prior to the injection, no blood was noted on aspiration of the syringe, nor was blood seen on the needle or in the syringe after injection. About five minutes after the injection, while en route home, he became short of breath and was immediately seen by one of us (D. L.) in the office. The patient was wheezing heavily and had a generalized erythematous rash on his torso.

Examination of the lungs revealed multiple sibilant rales throughout both lung fields. Frank pulmonary edema developed rapidly, with the appearance of white froth on the lips. A generalized convulsion occurred shortly thereafter, with loss of consciousness and apnea for about 30 seconds. During this time the pulse became imperceptible. The body skin became cool and appeared to be bloodless, and the lips and tips of the fingers became deeply cyanotic. He was immediately given 100 mg. of hydrocortisone sodium succinate (Solu-Cortef) and 0.5 cc. of epinephrine intravenously. After several gasps he regained consciousness and once again began to wheeze. About one minute after he had returned to consciousness his blood pressure was 100/70 mm. Hg. His heart rate was

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From the departments of medicine and surgery, Sequoia Hospital.

100 beats per minute and was regular. The skin remained blanched, possibly due to the effects of the intravenously given epinephrine.

Five minutes later 1 cc. of epinephrine was administered subcutaneously and another 100 mg. of hydrocortisone sodium succinate was given intravenously. Ten minutes after return to consciousness he was coherent and vomited about 300 cc. of yellowish clear fluid, but he felt quite well. One half-hour after the episode the heart rate was regular, at 80 beats per minute. His blood pressure remained stable. Due to persistent wheezing, the patient was hospitalized and gradually recovered, with continued administration of epinephrine and corticoids. No history of asthma or allergy was obtained.

Summary

A patient had a severe anaphylactic reaction to the intramuscular administration of aqueous chymotrypsin (Chymar). No similar case has been found in the literature to the time of this writing. It is believed worthwhile to record this reaction in order to alert other members of the medical profession, should similar experiences be encountered with further use of this drug.

90 Birch St. (Dr. Liebowitz).

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COMMITTEE ON COSMETICS

Report to the Committee

The following paper was presented at the symposium, "The Management of Cutaneous Facial Disfigurements," in Atlantic City, June 9, 1959. This symposium was sponsored by the Committee on Cosmetics at the 108th Annual Meeting of the American Medical Association. This is the second in a series of papers, the first of which appeared in THE JOURNAL *on Dec. 26, 1959, pp. 2326-2331.*

VERONICA LUCEY CONLEY, Ph.D., *Secretary.*

SURGICAL APPROACH TO FACIAL SCARRING

George F. Crikelair, M.D., New York

It is seldom possible in medicine or surgery to say "always" or "never." As far as it is possible to use either word medically, it seems reasonable to state that any patient seeking medical advice about an undesirable facial scar always wants it completely removed, and every surgeon making a facial incision, suturing a facial laceration, or removing an unsightly facial scar never wants to produce anything but an invisible scar.

The surgical approach to facial scarring is a vast topic, and, since it cannot be completely discussed in a short paper, only some of the basic factors involved in both the formation and surgical treatment of facial scars will be considered here.

A basic principle frequently unknown to most patients, especially those who read about the wonders of plastic surgery in the lay press, and a basic principle frequently forgotten or ignored by some physicians, is that each cut in the skin, regardless of where it is placed or who makes the cut, heals in the same manner as every other cut. That is, there is an inflammatory response to cuts, with the eventual formation of scar tissue. This is a basic principle in regard to facial scarring. Every cut or incision produces a permanent scar. However, in striving to make facial scars unnoticeable, there are surgical fundamentals which are helpful. None of these are new; they are the old and basic fundamentals of all such surgery.

1. If an incision is to be made on the face, the resulting scar should fall in the skin tension lines.[1] These lines follow a similar pattern in all people but may vary slightly from patient to patient. In general, the skin tension lines run perpendicular to the direction of the muscle pull. The direction of these lines can best be determined by asking the patient to wrinkle his face. The lines usually stand out clearly. In elderly people these lines are readily seen. This is not true in children. The face is fuller, and the skin has less tendency to form creases. Therefore, the surgeon must know the usual direction of the skin tension lines and attempt to follow them.

2. The edges of incised skin should not be mishandled or roughly treated; the tissues should be handled gently.[2] Clamps or heavy retractors should

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not be used on the skin edges. Small rakes or hooks are surgically helpful, but care must be taken not to add tissue damage which can lead to tissue necrosis.

3. The skin edges should not be sutured under tension. The cut skin edges on the face can be widely undermined along the subcutaneous plane which stretches the skin. If the skin is sutured under tension, the skin edges will have a tendency to pull apart. The scar will spread, and the sutures, being fixed structures in a given area, will cut through the tissues. This has been called extrinsic tension.[3] These tears, caused by the sutures, will result in linear scars perpendicular to the main line of the scar itself. Thus, the result will be a spread main scar, with smaller scars at right angles to the main scar.

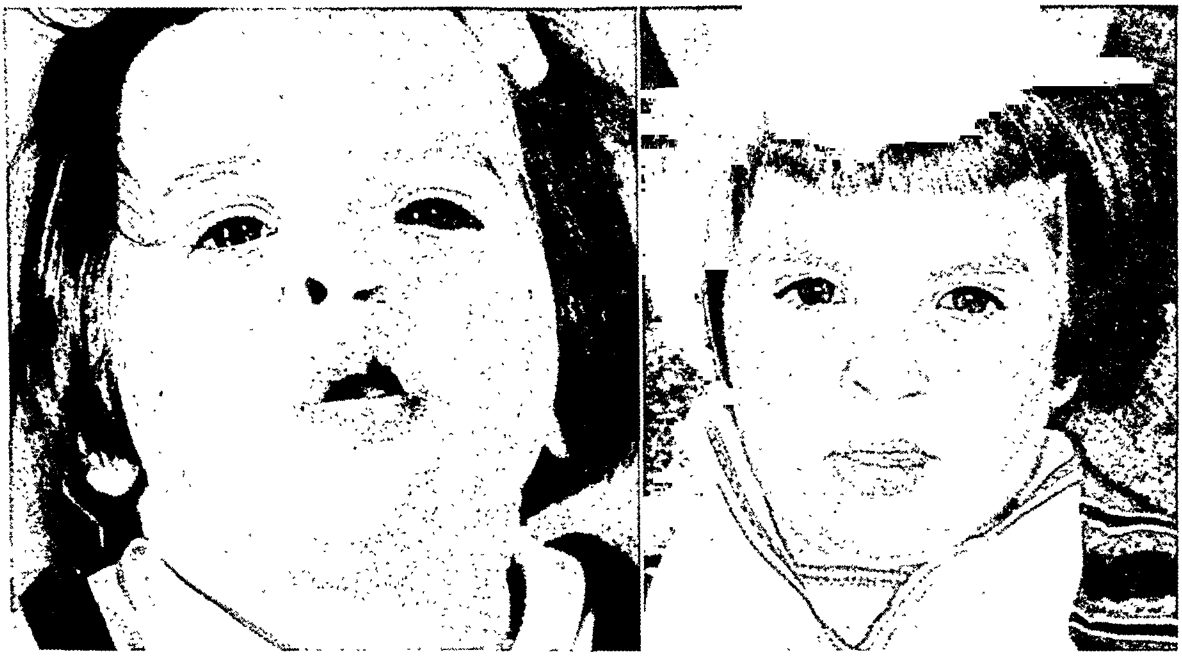

Fig. 1.—*Left,* patient after primary repair of complete left-sided cleft of the lip. Nasal ala and vermilion are not in normal alignment. *Right,* scar less noticeable after proper anatomic alignment.

4. Skin sutures should not be tied tightly. If they are, a vascular necrosis at each suture site will result. This has been called intrinsic tension.[3] As the sutures pull through the skin edges, there follows the same type of tissue necrosis, with a wound similar to that resulting from the suturing of skin edges under tension.

Subcuticular sutures will absorb tension on sutured skin edges.[2] The skin sutures are meant merely to lightly coapt the skin edges. Tension on a sutured wound can further be relieved by adhesive-tape butterflies and by large dressings which help immobilize the sutured tissues.

5. There are certain areas of the face which rather consistently result in less noticeable scars than others. For example, incisions in the eyelids usually heal, leaving fine, practically invisible scars. The same can be said of the preauricular region, which is the site chosen in doing a face-lift operation. The forehead usually heals nicely, despite the fact that a cut or incision may be perpendicular to the skin tension lines.

Other areas are not so kind to the surgeon. For example, scars over the lower third of the nose often become depressed. Scars about the chin are apt to spread. Also, certain diseases, such as lymphangioma, predispose to bad scars.

6. The idea is frequently presented that scars in children heal better than in adults and that the scar is therefore less noticeable. It is perhaps true that children develop tensile strength in a sutured wound more rapidly than does an adult, but, in this process, the scars are usually redder, more indurated, and, as regards the immediate postoperative appearance, much more noticeable than a comparable scar in an elderly patient. If a surgeon wants to get the best cosmetic result from a facial incision in the least possible time, he should choose a patient closer to the age of 90 years than 9 days.

7. The passage of time is perhaps the best, the kindest, and the easiest treatment to give to any facial scar of recent origin. But how many times are surgeons asked to see patients with facial scars weeks to months after an automobile accident! The surgeon, the patient, and the family may be disturbed about the scars. The scars may be red and indurated and rather bumpy and uneven. Most scars will improve, if given the time to do so. It may require 6 to 18 months for this gradual improvement to reach its maximum. When a scar is soft and white, the healing process has completely subsided. The time required for this varies from

person to person. Only after this point has been reached should surgical revision of a scar be undertaken.

Facial scars are noticeable if they result in an uneven surface or a poor color match, if they cause distortion of the surrounding structures, or if normal structures are malaligned.

The tightening of a straight-line scar through a free unattached structure such as the lip or eyelid may result in a contracture. This usually does not improve appreciably as time goes on. An example is the straight-line contracture in a repair of a cleft lip. Because of this contracture possibility, an attempt should be made to break these lines so the resultant scar cannot contract. Straight-line scars traversing the normal skin tension lines on the cheeks will often contract and cause hypertrophy. This can be prevented by placing incisions in the skin tension lines. If the scar is already present, the directional contracting forces can be changed by Z-plasties or multicurved incisions. Tissues obviously anatomically malaligned will not fall into normal position, and so early replacement is indicated (fig. 1). "Trap door" scars have a tendency to elevate the tissue encompassed by the scar, with a depression of the scar itself. These lines need to be broken either with Z-plasties or multicurved incisions to better distribute the contracting lines of force. A scar may be noticeable because it is depressed. This depression can be due to an underlying bony deficiency which must be repaired. Occasionally, there may be a deficiency of tissue so that skin from a neighboring area should be moved into place, or a free skin graft may be needed (fig. 2). A scar may be flat but hypopigmented or hyperpigmented. This may be due to absence of normal skin pigments, too much pigment, foreign body carbon particles, or the condition of the skin about the scar. In all these instances, make-up ranks very high in the therapeutic armamentarium.

A "good" facial scar would be one which is a fine line, level and even with the surrounding surface, the same color as the surrounding skin, and which causes no contracture or pull on the surrounding facial structures. Unsightly scars can be surgically corrected, and good results can be achieved by well-planned and carefully executed surgery.

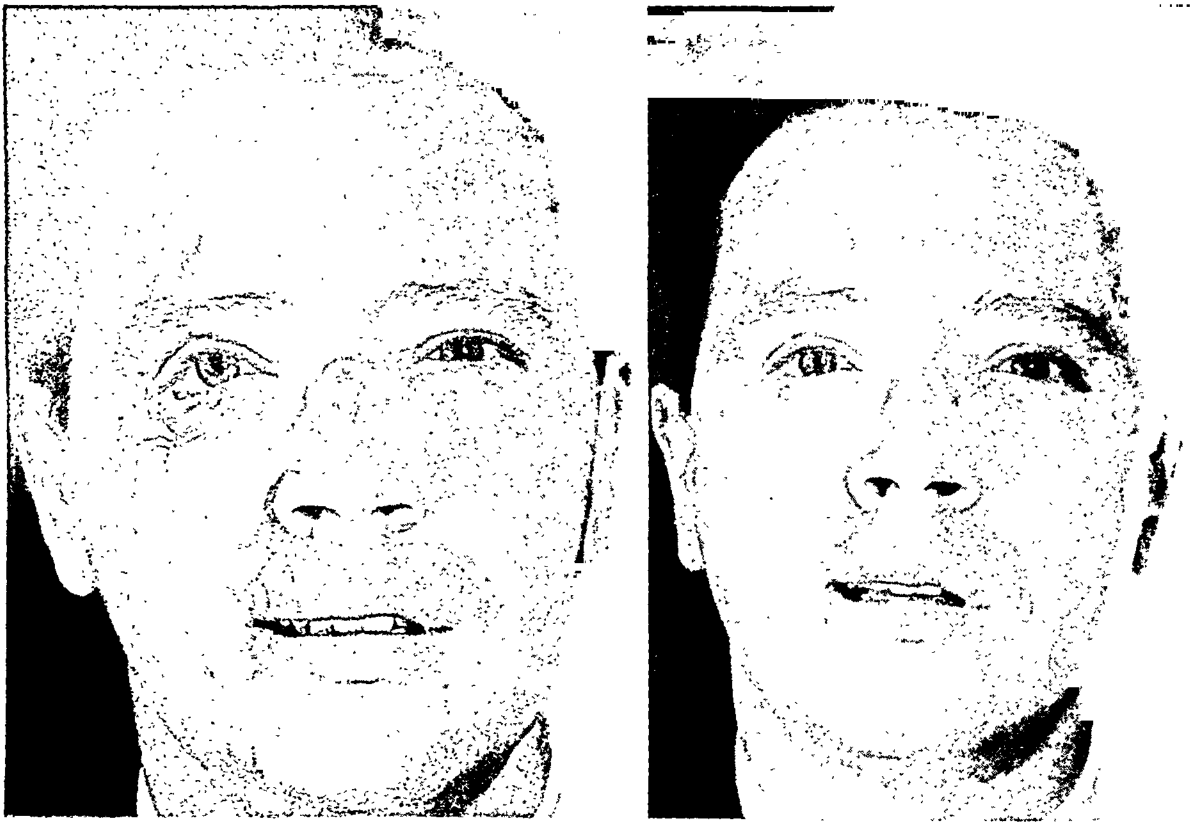

Fig. 2.—*Left*, patient with numerous scars on right side of face. Ectropion of right lower lid and right upper lip are most noticeable. *Right*, full-thickness postauricular skin graft used to correct ectropion of lid. Local skin flaps have been used to reposition right side of upper lip. Note how other facial scars have improved in six-month interval between photographs.

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COMMITTEE ON REHABILITATION

REHABILITATION PROGRAM IN ONTARIO FOR OCCUPATIONAL INJURIES

Earl C. Steele, M.D., Ontario, Canada

The following report is the fifth in a series of articles which have been authorized for publication by the Committee. The first four appeared in The Journal *on Oct. 24, Nov. 7, Nov. 21, and Dec. 12, 1959, pages 1107, 1359, 1694, and 2098. This series deals with various aspects of rehabilitation which are of interest to physicians.*

Ralph E. De Forest, M.D., *Secretary.*

In Ontario the Workmen's Compensation Board is charged with the responsibility of the rehabilitation of the industrially injured. The Compensation Act was primarily designed "to get rid of the nuisance of litigation" and "to have swift justice meted out to the great body of men" who have been unfortunate enough to suffer industrial disease or injury arising out of, and in the course of, employment. The act is administered by a board of commissioners who have been given broad administrative powers by legislation to effectually interpret the spirit and intent of the act. The board is a body corporate of three members who are appointed by the Lieutenant-Governor in Council. They have power to make regulations within the meaning of the act, but amendment of the legislation is the function of the Provincial Government. The board has exclusive jurisdiction in all matters pertaining to compensation, and there is no appeal to the courts. By statute the decisions of the board are not bound to follow strict legal precedent, and the act states that "the decisions of the Board shall be upon the real merits and justice of the case."

Unimpeded by legal quarrels in the courts, divorced from political interference, and invulnerable to vested interests with the profit motive, the board can concentrate its efforts and focus its attention on what we have long considered to be the goal of the compensation process—successful rehabilitation. Our objective in every case is to assist the injured workman to return to his job as quickly as possible, with minimum impairment.

The projection of this compensation philosophy has resulted in Ontario's adopting a biological or clinical approach to the compensation process rather than an adversary or forensic system. Rehabilitation in the broadest meaning of the term is an indivisible and integral part of the entire compensation system. We, like other observers, have been unimpressed by the results of attempting to graft a rehabilitation program onto a purely forensic system, which inhibits the rehabilitee from accepting such service until court settlement is completed.

I shall attempt to describe our rehabilitation efforts under the headings of medical care, physical medicine, vocational rehabilitation, and financial rehabilitation.

Medical Care Program

We believe that the rehabilitation of the injured is a continuous process, influencing the patient from the time of injury to the point of gaining independence and returning to work. There can be no gaps. If rehabilitation is viewed merely as a salvage service, it immediately loses a great deal of its effectiveness. Expert medical and surgical care, in our opinion, is one of the most important features in a planned rehabilitation program.

Breakdown of Rehabilitation Officer's Work with 341 Patients for One Year

	Cases, No.
Type and Site of Injury	
Arms and hands	85
Back	73
Legs	70
Chest	17
Dermatitis	16
Burns	10
Eyes	7
Paraplegic	5
Other	58
Total	341
Clinical Disabilities	
15% and more	110
Less than 15%	231
Total	341
Trades	
Skilled	54
Semiskilled	76
Unskilled	211
Total	341
Age Factor	
Under 50 yr.	259
50 Yr. and over	82
Total	341
Reemployment	
Former employer	153
Elsewhere	114
Retired	21
Pending and under treatment	53
Total	341

In Ontario, the Compensation Board has been given the responsibility by statute to control and supervise medical care in cases coming within its jurisdiction. The board has delegated this responsibility to the medical profession and allows workmen the initial free choice of medical attention. The physicians and surgeons throughout the prov-

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Commissioner, Ontario Workmen's Compensation Board.

ince know we want and demand the very best of medical care, regardless of cost. They know it is our policy to permit only those surgeons holding specialty certification from the Royal College of Surgeons to do major surgery. They know they can have unlimited consultation with their seniors. They understand that they can take all the x-rays required and repeat them when necessary, and that they may carry out any laboratory or special investigation considered helpful. The physicians are aware that they can pick up the telephone, reverse the charges, and discuss their problems with a qualified surgeon or internist on the staff, and that they will receive courteous advice. In the small urban centers and rural districts dotted throughout Ontario, physicians know that, in serious cases, we either will send from our University hospital whatever kind of specialist is required—plastic, orthopedic, or neurosurgeon—or will provide transportation at a moment's notice to bring the patient to one of the larger centers where specialized help is available. In order to assist the attending surgeon and to ensure adequate treatment, all preoperative and postoperative x-rays (500 to 600 per day) are sent to our head office where they are screened, photographed, and returned. Serious cases are discussed with our consultant radiologist and orthopedic surgeons. Problem patients coming from districts where specialized facilities are not available are transferred to the closest university center.

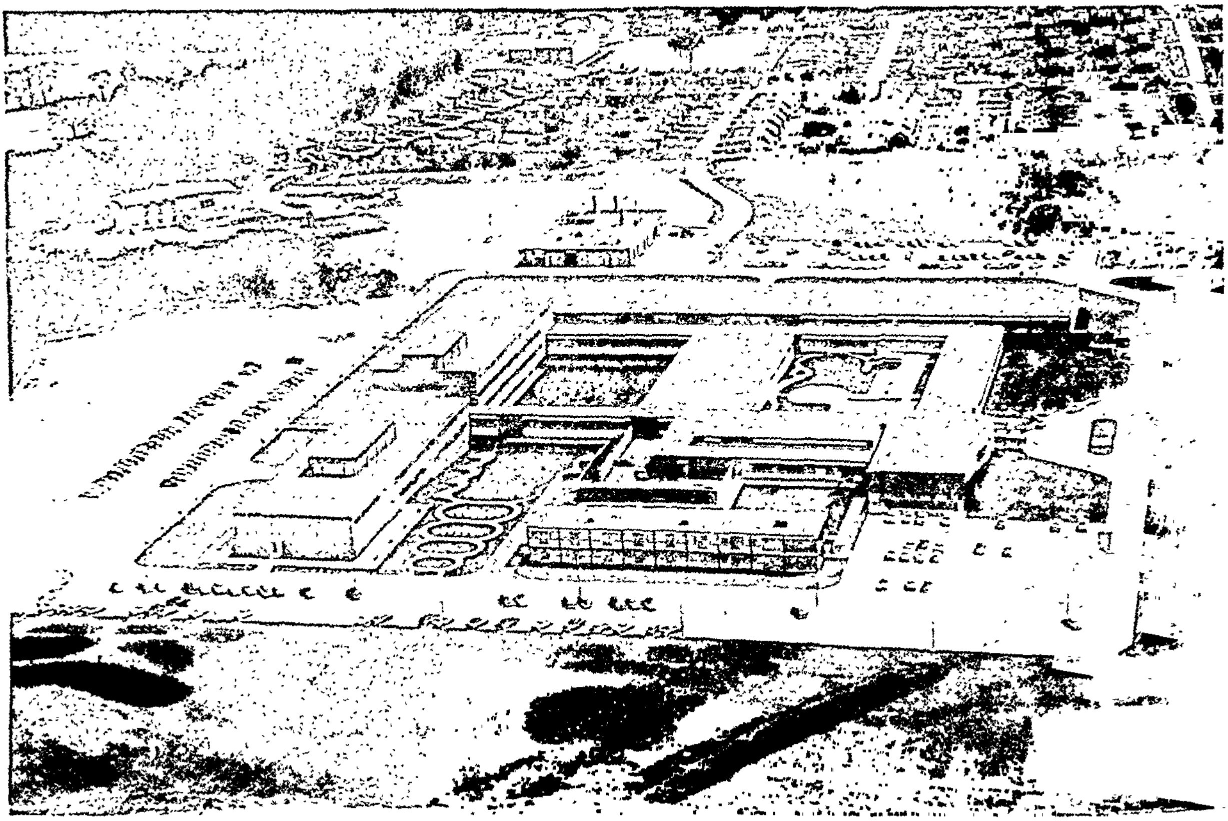

Fig. 1.—Workmen's Compensation Board Hospital and Rehabilitation Center, Downsview, Ontario.

We rent, on a yearly basis, a floor in our largest teaching hospital for the more serious and complicated surgical and orthopedic cases. Here we control admissions and discharges. We also maintain a block of beds and a specialized team for the care of paraplegics.

The co-operation and enthusiasm of the medical profession for our plan has contributed, to a large extent, to any success we may have gained in our attempt for early rehabilitation through a definitive medical care program.

Physical Medicine

Supervised physical and occupational therapy have played a vital role in our rehabilitation program, inasmuch as restoration of function is one of the cardinal aims of treatment. Our experience in this field dates from 1932—27 years ago—and had its starting point in a small room in our downtown compensation office. Facilities have been gradually expanded and enlarged, culminating in a recently opened 550-bed hospital, with 65 acres of ground on the outskirts of Toronto, which was established as a rehabilitation center for patients receiving workmen's compensation (fig. 1). This functional building consists of a hospital section for the care of early convalescent traumatic patients received from general hospitals and a clinic section for ambulant patients. All our patients are referred through the board's medical department by physicians throughout the province. The referring physician is informed biweekly of the patient's progress and is given a resumé of the findings and recommendations for further treatment or rehabilitation measures to be undertaken on discharge.

The staff at the hospital and rehabilitation center are 300 in number and include 12 full-time doctors, 23 registered nurses and 20 assistant nurses, 22 physiotherapists, 21 occupational therapists, 9 remedial gymnasts, 3 psychologists, 2 consultant orthopedic surgeons, and a radiologist. Planned and supervised activity is the keynote of treatment. On admission, each patient is seen by a physician and a rehabilitation officer, along with his complete record of previous treatment, x-ray findings, work history, and social background. It is the duty of the rehabilitation officer to locate employment problems and to keep the employer informed regarding return to work and whatever job modifications may be required. When additional placement services are needed, referral is made to a field rehabilitation officer for follow-up.

After examination and diagnosis, a detailed prescription is planned for a seven-hour daily program, including physiotherapy, remedial gymnastics, occupational therapy, hydrotherapy, and recreational activities (fig. 2 and 3). Cases are reviewed by staff physicians at weekly intervals, and prescriptions are changed or modified according to the patient's progress. Monthly case-evaluation conferences are held regarding each patient, with all members of the team present. In both the hospital and clinic section, the patient follows a daily program of progressively graded individual and group activities designed for restoration of function, reeducation of lost skills, regaining of confidence and preparation for return to independence, and useful community living. When the question arises regarding the ability of a patient to return to his former job, a work-assessment test is carried out in the occupational therapy department. Patients are assigned to tasks which simulate actual work conditions and, when possible, with the tools of their own trade such as bricklaying, carpentry, telephone linemen, laying railway ties, or pushing loaded ore carts (fig. 4).

If change of job or retraining is necessary because of resulting disability, the rehabilitation

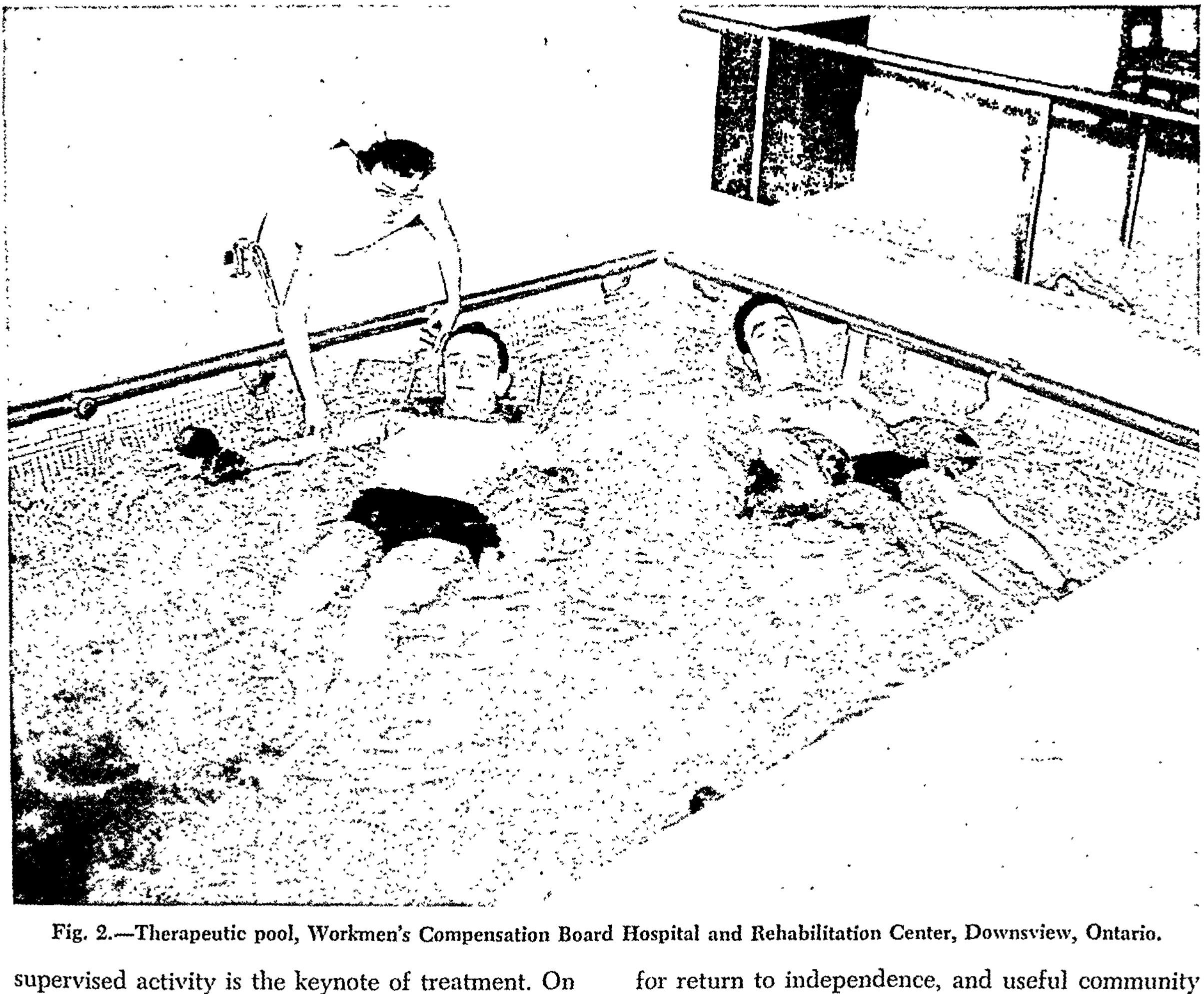

Fig. 2.—Therapeutic pool, Workmen's Compensation Board Hospital and Rehabilitation Center, Downsview, Ontario.

counseling service evaluates intelligence, vocational aptitudes, background experience, and personality traits. A small, self-contained unit within the center deals with those patients requiring specialized help to overcome emotional instability, hysteria, or neuroses.

Vocational Rehabilitation

Like other observers, we believe that any organized plan for the restoration of the injured should be made on the basis of the following theories: rehabilitation always, resettlement sometimes, and retraining as infrequently as possible. In our experience the vast majority of those injured in Ontario wish to return to their old or modified jobs with their former employer. Lack of education, inability to learn new skills, language barriers, middle age, and doubtful adjustment to new environment usually make retraining impractical, costly, and wasteful. Prevocational guidance and counseling are carried out by our vocational rehabilitation department. For actual retraining we use existing facilities in the province, e. g., business colleges, electronic and welding schools, barber colleges, and institutions offering engineering courses. Our compensation law gives the board the right to spend up to $200,000 per annum toward this end. Last year about 80,000 men were injured in Ontario, necessitating a layoff from work of more than four calendar days. Retraining was carried out in 91 cases only.

Our rehabilitation staff at the hospital and rehabilitation center and field men located in various cities throughout the province attempt to make early contact with the more seriously injured. Their rights under the act are explained, their doubts and anxieties are relieved, and their misgivings concerning the future are dispelled. The rehabilitation staff member offers reassurance and acts on behalf of the board as friend and adviser. Early contact is also made with the local union representative and with the employer. A promise of reemployment after severe injury often protects the patient against neurosis and hastens his return to work.

A typical breakdown of a rehabilitation officer's work for one year is shown in the table. The patients who presented the greatest difficulty in job placement were those in the unskilled and advanced age groups. Placement was also difficult and time-consuming for workmen who had had previous disabilities and spotty and unsatisfactory work records. Seasonal workers or transient laborers presented a peculiar problem in job placement. The handicapped persons suffering from back injuries, dermatitis, and head injuries were extremely hard to deal with.

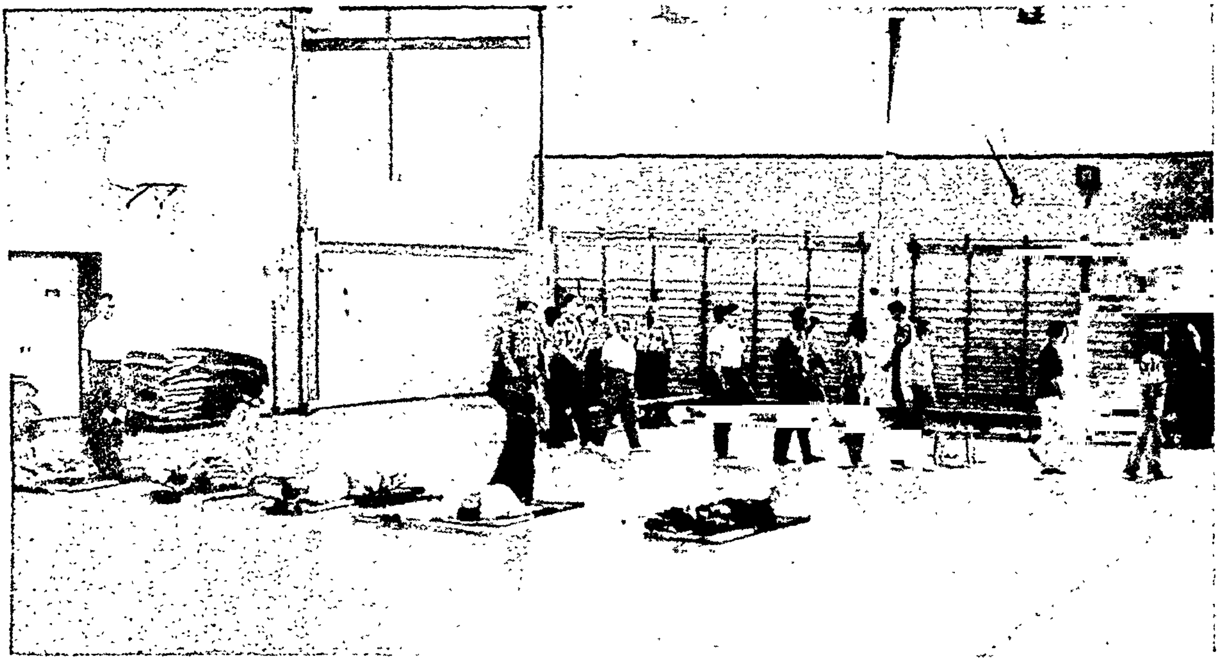

Fig. 3.—Group therapy by remedial exercise, Workmen's Compensation Board Hospital and Rehabilitation Center, Downsview, Ontario.

Other Rehabilitation Services

In our opinion, rehabilitation should be a "grass-root," hometown affair whenever possible. Leadership should be given by the local physician, and general hospitals should be equipped to handle all but the more serious rehabilitation problems. Our policy is to buy services where facilities are adequate and to reserve the Compensation Board Hospital and Rehabilitation Center for the more serious or problem cases. Specialist services are available from other agencies. Prostheses are obtained through our Veterans' Affairs Administration. Speech therapy is purchased from private practitioners. Blinded workmen are referred to the Canadian Institute for the Blind. The Canadian Hearing Society assists with the rehabilitation of those with impaired hearing. Cases of paraplegia are sent to Lyndhurst Lodge, operated by the Canadian Paraplegic Association. Other community rehabilitation agencies including the Special Placement Division of the National Employment Service are utilized on occasion.

Fig. 4.—Patients exercising under supervision of an occupational therapist.

Financial Rehabilitation

Prompt, regular payment of compensation during periods of incapacity is an important factor in the rehabilitation process. Doubts and fears should be prevented if at all possible. The patient must not be allowed to be concerned about financial hardship during the course of his total disability nor to have fears and forebodings for the future. When an Ontario workman is off work for more than four calendar days as a result of injury, he is entitled to 75% of his weekly wages (to a maximum of $5,000 a year or $72.11 a week) as long as total disability lasts and during the period of retraining, if the circumstances demand such extra payment. He is entitled to all necessary medical aid, unlimited as to time or amount. Prostheses are furnished and replaced when necessary or are kept in repair during the lifetime of the claimant. Permanent disability pensions are paid for life, regardless of the man's earnings.

Summary

The Ontario plan of compensation, based on a clinical rather than on an adversary approach, is, in effect, a large-scale rehabilitation effort. The individual physician plays a vital role in a team effort to return injured employees to the job quickly, with minimal disability. Our concept of rehabilitation includes skillful medical attention at the outset, along with all the skills, modalities, and techniques available to restore the patients to their pre-accident state. From our experience over the years, we are convinced that this approach is more humane to the injured workman and less costly to the employer. Those groups of the community most vitally interested—organized labor, employers, and the medical profession—endorse our rehabilitation-compensation system.

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GOUT AND BLOOD DYSCRASIAS

THE best evidence to date suggests that in patients with familial gout the metabolic alterations are related in large part to an overproduction of uric acid. Furthermore, a considerable volume of experimental data has been accumulated which shows that patients with various blood dyscrasias develop a disturbance of uric acid metabolism that is clinically, histologically, and in some stages biochemically undifferentiable from that observed in patients with familial gout.[1] Basically, however, the mechanism is different. The increased concentration of serum uric acid and the increased excretion in the urine follows an increased formation and destruction of red and white blood cells and an increased metabolism of nucleic acids in the blood-forming organs with the elaboration of intermediary products of purine metabolism. Such patients are susceptible to a sudden onset of acute distress associated with the cardinal signs of inflammation in one or more of the distal joints of an extremity. The symptomatic response to colchicine, prescribed in full doses, is excellent. The clinical findings, together with the therapeutic response to colchicine, are sufficient to justify a presumptive diagnosis of gouty arthritis. Roentgenographic changes in the bones and the presence of tophi are confirmatory evidence but are not required for diagnosis.

On casual inspection it might appear that the patient was merely suffering from gout superimposed on the inherent blood disease. An understanding of the mechanism described above and the awareness that the association of gouty arthritis with hemopathies is significantly greater than the association with nonhematological disease constitutes a strong argument in support of a causal relationship. An underlying blood dyscrasia may be present in a significant number of patients suffering from clinical gout. Also, an occasional patient with familial gout may develop a hemopathy. One confusing aspect of such a development is the possibility that the hemopathy has been asymptomatic or in a subclinical stage for a long time. Thus, an increase in the serum uric acid level may have been the first manifestation of the underlying blood disease.

Although a number of blood diseases, in comparative study, were found to be associated with gouty arthritis, the most frequent was polycythemia vera. There is no evidence that a fixed organ malignancy or a blood dyscrasia which develops sometimes in patients with gout is due to the colchicine prescribed prophylactically.

The status of the red and white blood cells should be reviewed from time to time in patients with clinical gout; per contra, a patient with a blood dyscrasia who complains of joint pains should be under some suspicion of suffering from clinical gout.

TRIVIAL AND IMPORTANT ERRORS

The question is whether men are bound to act like robots when they can set themselves independent goals that are preferable. In dealing with error, Intellect is able to discriminate between trivial and important. Modern readers, as we know, take all facts as equal and rush to fill the correspondence columns with indignation whenever they catch any small mistake in print. For these slips, writers and editors apologize with a humility not seen on earth since the early Church. The expensive apparatus for detecting error before publication grows nearly infallible about trivia, and nearly blind about what matters. A wrong initial in some obscure name is set right, while a colossal nonsequitur is overlooked. In the end this unsuspected lack of balance regulates (if that is the word) the public mind, which then wonders at the state of our education and the qualities of our politics.—J. Barzun, The House of Intellect, New York, Harper, 1959.

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[1] Talbott, J. H.: Gout and Blood Dyscrasias, Medicine 38:173-205 (May) 1959.

COUNCIL ON MEDICAL SERVICE

HOW SICK ARE OLDER PEOPLE?

Ethel Shanas, Ph.D., Chicago

The medical practitioner, the hospital administrator, the visiting nurse, or the family social worker, all of whom see an increasing number of older people in need of medical care or services, probably would answer the question "How sick are older people?" with an overwhelming consensus: "Older people are very sick." The 15 million people 65 years of age and over in the United States, and those relatives and friends to whom older people would turn in a health crisis, however, give a different answer to this question. Most older people, as many as 8 or 9 of every 10, would say "I've a lot of things wrong with me, but I'm not really very sick!"

Only a small proportion of the 15 million older people in the United States are in institutions. The number in institutions has been estimated at between 450,000 and 750,000, or from 3 to 5% of the older population. The exclusion of this small group from the study probably means that those among the aged who are physically most seriously deteriorated have been omitted from this investigation. Findings from the sample, however, may be generalized to the total older population of the United States living outside of institutions.

The general picture which emerges from the responses of older people and their interested relatives is that of an older population with many complaints but relatively few serious enough, from the point of view of the respondents, to require medical care. Seventeen of every 20 older persons said that they had been ill during the four weeks preceding the interview. "Illness" was defined as any condition, that is, any disease, injury or impairment, symptom, or group of related symptoms which the respondent said had "bothered" him. The questions on illness, although not as extensive, were comparable to those of the National Health Survey. Half of all persons interviewed said that they had suffered from diseases of the circulatory system during the four-week period preceding the interview; one-third reported illness involving diseases of the bones and organs of movement. The average number of illnesses for the four-week period were four per person.

Despite the large number of illnesses reported, about two-thirds of the people with illness said that their illness had interfered in no way with their normal mode of behavior; they were neither kept in the house, restricted from climbing stairs, confined to a wheelchair, nor kept in bed. Only one in eight of the total group who said they had been ill, that is, about 1 in every 10 persons in the total older population, had spent one or more days in bed during this four-week period. Further, only one person in three of the group who said that they were ill had seen a doctor or talked to him on the telephone. Ten per cent of the small group who said they had not had an illness episode during the four weeks preceding the interview had seen or talked to a doctor during this period. Such persons, of course, may have had long-time chronic conditions which had not "bothered" them during the four-week period but for which they were receiving medical attention.

Without further analyses, these self-reports of illness among the older population may seem contradictory and disturbing. If 17 of every 20 people aged 65 years and over report something wrong with them during a four-week period, why is it that only one-third of those who are ill, only about 6 of every 20 people in the older population, have seen a doctor or talked to one over the telephone?

First, despite the large number of reported illnesses, most older people do not think they are sick. Half of all persons aged 65 years and over report their health as "good," and half of them say their health is better than that of other people their age. Evidence that these self-reports are fairly realistic self-assessments comes from interviews with relatives and friends of the older people interviewed. Half of all relatives and friends of older people report their older relatives' health as "good" or "good for his age." Further, two-thirds of all relatives and friends say that their "older person" sees a doctor less often than do most people his age. Then, too, it should be realized that most of the illnesses reported by older people are chronic illness and impairments of long duration. Half of the total illness reported by older people as having "bothered them" were illnesses which they said they had had for five years or more. Older people take such illnesses for granted. Indeed, three of every four respondents believe that "older people have to expect a lot of aches and pains."

Senior Study Director, National Opinion Research Center, Research Associate (Associate Professor), Department of Sociology, University of Chicago.

Read before the meeting of the Committee on Aging, American Medical Association, Minneapolis, Oct. 14, 1959.

Finally, older people usually will not see a doctor unless they experience an acute illness episode. An analysis of the reasons why two-thirds of the people who said they had been ill had not seen a doctor reveals an attitude toward health problems which may differ from that of the general population. First, most of these older people, regardless of the nature of their illness, said they did not feel sick enough to see a doctor; second, most of them believed that they could treat the illness as well as a doctor could. It should be kept in mind that two of every three older people believe that "a person understands his own health better than most doctors do." Only one person in 16 mentioned lack of money as a reason for not seeing a doctor. Later in the interview, however, when asked "Are there any things you especially need that you've had to do without because you don't have enough money?" about one person in 12 in the total sample voluntarily mentioned medical care, dental care, or medicines.

In separate interviews, relatives and friends of older respondents were asked whether they believed that these older persons saw a doctor as often as they should. One of every three relatives said "no." Relatives and friends reported that money was not the main reason older people did not see the doctor, although more relatives than older people mentioned finances as a deterrent to medical care. The primary reason why relatives and friends felt their old people did not see a doctor was that "their older person" would not see a doctor unless he or she believed he was seriously ill.

How sick, then, are older people? The National Opinion Research Center findings indicate that the very sick among the older population comprise about 10% of all the persons interviewed. If those people located in the general population who were "too sick to be interviewed" are added to this group, this proportion rises to 14%. The "very sick" in the older population are estimated to be from 9 to 11% of those aged 65 to 74 years, or about one in every 10 in this age group, and from 14 to 20% of those aged 75 years and over, or at most about one in every 5. The lower proportions are based only on those interviewed in the study; the higher proportions include those "too sick to be interviewed" but located in the noninstitutional population. In the total population aged 65 years and older, the "very sick" may be found among women, 75 years of age or more, living primarily in rural counties. These estimates are based on the total group: those interviewed, plus those "too sick to be interviewed." The rest of the older population, some 13 million persons, may suffer from substantial illness and impairment, but nevertheless three of every four agree: "The way things are now people can expect to feel pretty good when they're 70."

COUNCIL ON NATIONAL DEFENSE

UTILIZATION AND TRAINING OF PARAMEDICAL PERSONNEL

Lieut. Col. H. Haskell Ziperman, Major Theodore H. Nicholas
and
Col. Walter D. Spearman, (MC), U. S. Army

Disparity between total number of casualties and the medical means available for their treatment will be the problem facing us in the event of thermonuclear warfare. It is probable that millions of casualties will then be simultaneously produced throughout the length and breadth of the country. In fact, for the first time since the Civil War our country and our civilian population will be just as susceptible to destruction and injury as are our military forces. It has been estimated that the disaster in such a situation can develop to the point to which each physician will have to provide simultaneous care for as many as 500 casualties and that this care will have to be provided with grossly inadequate supplies and equipment.

Medical Management

The medical management of large numbers of sick or injured involves the establishment of an organization which takes into consideration every essential of proper care. This orderly process of medical management insures that we will not jeopardize the lives of many in order to care for one or a few injured and permits us to minimize the time lag between injury and the institution of appropriate therapy. This is the basis for the military medical organization which handles casualties during wartime. That it functions well and does the greatest good for the largest number of injured is proved by the mortality of 4.5% obtained during World War II and the phenomenonally low mortality of 2.4% during the Korean War. Taking this into consideration, the Office of Civil and Defense Mobilization has patterned its medical plan for

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Lieut. Col. Ziperman is presently assigned as Chief, General Surgery Service, Letterman Army Hospital, San Francisco.

disasters on that of the Army Medical Service. The conventional medical plan of the military, however, is established in such a way as to provide adequate supplies, personnel, and equipment to handle all foreseeable casualty loads. Only occasionally will the number of casualties produced exceed medical capabilities, and in those situations additional facilities usually can be mobilized quickly. However, in case of mass casualties resulting from thermonuclear warfare or other large scale disaster, the situation depicted above will not exist and some means must be provided for reducing the expected disparity between medical work load and available medical resources.

Various means for the reduction of disparity have been discussed and, in some instances at least, adopted by either the military medical services or the Office of Civil and Defense Mobilization. These include the following factors.

It is believed that by a decrease in population density the effect of either the natural disaster or the thermonuclear explosion will be minimized. This is feasible in military populations in the field because their locations are at the discretion of the commander. However, dispersion of units will bring into existence a new problem, namely, the necessity for transporting the wounded over relatively large distances when control of these areas and the air above may not be in the hands of the defenders. Among civilian populations, dispersion is a long-term procedure which can be accomplished only with difficulty at the time warning of impending attack is received.

Change in priority for treatment will include abrogation of the old principle of severity of injury determining urgency of treatment required. Substituted, therefore, will be the division of casualties into certain treatment categories with priorities for treatment being established on the basis of probability of survival. This will permit concentration of care on the 80% of casualties most likely to be benefitted and the relegation to the lowest priority for care of the 20% of casualties who are so critically wounded as to be likely to die in spite of care.

By the introduction of shortcuts and compromises in therapy more casualties can be treated per unit of time. Implicit in this idea is acceptance of an increase in morbidity, provided there is little or no increase in mortality. This can be accomplished by anticipating that at some future time resultant disability can be minimized with further corrective procedures.

Institution of survival care only indicates a defeatist attitude because it anticipates that only minimal treatment will be provided and that this treatment will be given only to those casualties who are likely to recover with this form of therapy. The other casualties would be permitted to die without a significant effort being made for their salvage.

In any natural disaster it is known, and in thermonuclear warfare it is anticipated, that a considerable period will intervene between the time casualties are produced and the time medical help becomes available. If this be true, the only care which can immediately be provided for these victims would be provided by lay persons in the disaster area. If maximum salvage of life and limb is to be achieved under such circumstances it is necessary that the present first-aid training program for firemen, policemen, Red Cross workers, and Boy Scouts be broadened to include the entire population. It is anticipated that this program can be introduced as a part of the curriculum of grammar schools, high schools, and colleges. This program should be a progressive one, in keeping with the intellectual capacity of the students involved for the absorption and retention of this instruction, and should include training in bandaging, splinting, control of hemorrhage, correction of certain respiratory defects, and alleviation of pain.

The greatest promise in the reduction of disparity is in a method which envisions the training of certain members of the healing profession in the performance of various emergency treatment procedures. The persons to be so trained would be dentists, veterinarians, nurses, medical technicians, and other so-called paramedical personnel. This type of training cannot be expected to provide medical and surgical judgment for the trainee, for judgment can be obtained only through clinical experience preceded and reinforced by adequate didactic background. In effect, with adequate training these paramedical personnel will provide additional pairs of hands for the physician who has the responsibility for saving life and limb and preventing clinical deterioration. In this way the physician will be enabled to carry out several treatment procedures simultaneously in the period of time in which he could normally carry out only one.

To be effective this training program for paramedical personnel must consist of demonstrations or practical exercises presented as far as possible on an individual rather than on a group basis. In addition, insofar as possible it should stress improvisation of medical means because of the expected shortage of supplies. Under no circumstances should this program be considered to be one of "upgrading" paramedical personnel, for in truth it consists merely of teaching a specific skill or group of skills which can be mechanically performed in order to save life or limb or aid in recovery. This does not suggest that these persons would necessarily know where or when these procedures should be accomplished, as this would require clinical judgment. Instead, the physician would make the decision and direct the assistant to perform the mechanical procedure, thus freeing the physician for other professional duties.

Duties of Paramedical Personnel

The specific procedures which paramedical personnel should be capable of performing are grouped into two general categories. Category 1 includes those procedures which may be performed without supervision by a physician, since their application requires little, if any, diagnostic skill and no surgical judgment. Category 2 should include those procedures which must be supervised and directed by a physician because the establishment of a diagnosis is required and the application of surgical judgment is necessary.

Category One.—Category I should include the following procedures.

Bandaging and Dressing of Wounds: Emphasis should be placed on the effective covering of wounds to prevent further contamination. Essentially, this training time should be devoted to a demonstration and practical exercise in how to apply a snug, protective, nonconstrictive dressing to any part of the body where a wound might occur. There is no need to teach refinements of bandaging technique such as spirals, spiral reverses, and others. While the use of manufactured dressings such as the Army field dressing should be demonstrated, emphasis should be placed on improvisation from available materials.

Splinting of Fractures: The principle of "splint them where they lie" should be taught. Improvisation of splinting materials, such as the use of boards, newspapers, pillows, and other materials, should be emphasized. The immobilization of the arm by tying it to the trunk and of the leg by fixing it to the other leg is of great value in such a situation. The use of manufactured and available splints such as the Thomas leg splint, basswood splint, and wire ladder splint should be demonstrated and, if possible, actually applied by the trainee.

Arrest of Hemorrhage: While the important procedure is the arrest of hemorrhage by the application of pressure bandages, the trainee should be taught pressure points and extremity elevation as temporary expedients until the proper dressing can be applied. In addition, the proper application of tourniquets should be taught with the full realization on the part of the trainee that the use of a tourniquet in a mass casualty situation will probably mean ultimate amputation of the extremity to which the tourniquet is applied.

Proper Positioning of Patients: Casualties may lose their lives because of improper positioning during transportation. This can occur in persons with fractures of the cervical or thoracic region of the spine who are moved without immobilization, in patients with maxillofacial bleeding who are carried in the supine position, and in patients with many other conditions. Emphasis should be placed on teaching of positioning to prevent deterioration of the condition due to interference with vital functions.

Infusion, Transfusion, and Injection Techniques: The proper method and materials involved in carrying out infusion, transfusion, and injection procedures should be taught. These should include sites of election for drawing blood and starting infusions and transfusions. Familiarity with supplies and apparatus available must be emphasized.

Artificial Respiration: Included in the period of performing artificial respiration should be simple procedures for reestablishing an airway. This includes the evacuation of blood, vomitus, and debris from the mouth and pharynx. Artificial respiration by the mouth-to-mouth technique should be the one which is taught.

Check on Vital Signs: Included in a check on vital signs should be a demonstration and practical exercise in taking and recording blood pressure, temperature, pulse, and respiration.

Operation of Resuscitative Apparatus: Operation of resuscitative apparatus should include training in the operation of oxygen therapy equipment, various types of suction equipment, the use and care of thoracotomy tubes, nasogastric tubes and Wangensteen suction, and the care of tracheostomy cannulae.

Preoperative and Postoperative Care: The need for the preparation of patients for surgical procedures should be emphasized. Emphasis should also be placed on the vital signs to be looked for to assure proper preoperative preparation and the postoperative recovery of a patient.

Aseptic Technique: Emphasis should be placed on knowledge of the principles of sterilization by moist and dry heat and by chemicals. Definition of a surgical field should be illustrated. The principles involved in the surgical scrub, and gown and glove technique, should be provided.

Catheterization: The proper technique involved in inserting a urinary catheter should be taught, and methods of continuous bladder drainage should be illustrated.

Category Two.—Category 2 should include the following procedures.

Thoracentesis for Hemopneumothorax and Intercostal Block: Under appropriate circumstances both thoracentesis and intercostal block are lifesaving procedures. Not only is a good deal of skill required to establish the proper diagnosis but proper insertion of the needle or needles in the appropriate interspace may have to be directly supervised by the physician. With practice, paramedical personnel can provide considerable assistance in the management of these victims of chest trauma, thus freeing the physician to care for more casualties per unit of time.

Cutdowns for Intravenous Therapy: Although a cutdown for intravenous therapy is a relatively simple procedure requiring little if any diagnostic skill in its application, a novice will have difficulty in determining the proper site for cutdown. In patients with severely burned extremities it may be difficult to find any patent vein. These difficulties and their solution should be emphasized to the trainee.

Emergency Tracheotomy: To be effective, emergency tracheotomy should be performed before the patient is *in extremis*. The decision to perform this procedure is one which requires surgical judgment and as such should be directed by a physician. In addition the technical skill involved is such that the procedure should be supervised by a physician at least until such a time as the novice has had an opportunity to perform it on several occasions without complications.

Simple Débridement: Considerable skill is required to perform simple débridement effectively. Paramedical personnel will require supervision at least the first few times they perform débridements. In addition, surgical judgment is required to determine whether and when this procedure should be carried out in a mass casualty situation. This is the most frequently performed surgical procedure for the victims of mechanical trauma in a disaster. If the procedure is adequately learned and performed by paramedical personnel, the physician is freed to concentrate on the technically more difficult surgery which other casualties will need.

Anesthesia: It is anticipated that only simple anesthesia techniques will be taught. These, for the most part, should include the open-drop ether technique. Because anesthesia machines and apparatus may be available and are simpler to use where this technique is well learned, the use of these machines should be taught. The signs associated with depth of anesthesia should be emphasized.

Aid in Sorting: The well-trained physician is the only person capable of making the life and death decisions required in sorting. Paramedical personnel should, however, be taught how to assist the surgeon in performing the procedures required. In order to do this, they should be taught the principles and aims toward which sorting is directed. This will greatly facilitate and speed up all sorting procedures. These persons will be particularly responsible for performing those activities directed by the physician so that he may continue sorting rather than become involved in treatment.

Suturing Technique: The learning of suturing techniques by paramedical personnel will permit the physician to go on to the next patient in the operating room sooner than he could if he were required to close all wounds himself. This permits the physician to take care of a larger number of surgical patients per unit of time.

Comment

A total of only 18 different subjects are listed in the two categories, and these can easily be taught to individual persons or small groups in a matter of 30 to 40 hours' training time. Not all procedures need be taught to all paramedical personnel. For example, the nurse requires no training in how to check vital signs or in principles of sterilization. All disciplines, however, can benefit from training in artificial respiration and bandaging and splinting. It should further be emphasized that this training is directed toward the carrying out of procedures and not the care of a specific clinical condition. The sum total of all these procedures will, however, permit nonphysician personnel to aid the physician in the care of any victim of trauma, be it due to burns, radiation, or mechanical injury.

As may be seen from the procedures outlined, emphasis is placed on those emergency life and limb saving measures which contribute significantly to a decrease in mortality in the mass casualty situation. Certain additional procedures are incorporated which are not directly life or limb saving but contribute to the recovery of the patient and his early return to a useful status. These serve to free the surgeon so that he may see and contribute to the survival of a larger number of casualties.

It must be emphasized that all of the procedures as listed fall within the province and responsibility of the physician in peacetime in a nondisaster situation. An occasional procedure has heretofore fallen within the province of the nurse. However, most, if not all, of these procedures have been delegated at times to properly trained medical aidmen in the combat zones of past wars. This has been shown to be practical, desirable, and necessary to help in overcoming the disparity of the medical workload to available physicians in time of heavy fighting. Since these procedures are the professional responsibility of the physician it should be up to him to decide to whom he is willing to delegate these responsibilities. In addition, it should be he who trains these paramedical personnel in carrying out these mechanical procedures. Unless the physician is willing to take the proper interest in teaching these various procedures, they will not be carried out at the proper time to his satisfaction.

It is unquestioned that in a mass casualty situation some type of physician assistance program will have to be instituted. Given any significant mass casualty situation, it is obvious that dentists or veterinarians, for example, could not be fruitfully engaged in their usual occupations nor would these occupations contribute significantly to recovery from the disaster. The abilities of these highly skilled personnel would be wasted in first aid, rescue, or labor activities. With their background in anatomy and physiology and their experience in dealing with pain and disease, these mature professional men represent our greatest and most promising source of manpower to increase our medical capabilities. Unquestionably we will be obliged to use them in rendering treatment in a mass casualty situation, but their potential contributions will be lost or at least blunted if we defer their training in these procedures until the casualties descend on us.

Toward this end then, the American Medical Association, the American College of Surgeons, and other policy-making medical organizations should take the initiative for the institution of this type of training. The various disciplines in the healing arts are ready to assist us in instituting some type of program among their members. They are looking to us for leadership and guidance in a training program which can be responsible for saving thousands of lives.

MEDICAL NEWS

CALIFORNIA

Funds Available for Cardiovascular Research.—The Los Angeles County Heart Association announced that applications for research funds from the Los Angeles County Heart Association must be received by Feb. 1. Applications will be accepted for fellowships, investigatorships, and grants-in-aid, according to Dr. Mitchel D. Covel, Beverly Hills, chairman of the association's Research Allocation and Policy Committee. Any investigator interested in cardiovascular research is invited to apply. Applications must be submitted in 15 copies. Interested scientists may write the Research Section of the association at 2405 W. Eighth St., Los Angeles 57, for a copy of the manual on research awards. This publication gives full details on policies and procedures for applications and granting of awards. The Heart Research Committee was reorganized during 1959 under the leadership of Dr. Covel. The committee now includes not only a research allocation and policy group with final responsibility for making research awards, but also three study sections to provide careful evaluation of each application received.

CONNECTICUT

Professor Hiscock to Retire.—Prof. Ira V. Hiscock will retire from his position as chairman of the Yale University public health department on Jan. 1. Dr. Hiscock, a member of the Yale faculty for 40 years, has been the Anna M. R. Lauder Professor of Public Health since 1945. Although not due to retire officially until June 30, 1960, Dr. Hiscock is being granted leave by the university for his last six months to assume a Carnegie Visiting Professorship in Public Health at the University of Hawaii in Honolulu. Dr. Hiscock served as president of the American Public Health Association in 1956-1957 and has served as president of the National Health Council and the Association of Schools of Public Health of the United States and Canada.

University News.—A portrait of Dr. Stanhope Bayne-Jones, Washington, D. C., who served as dean of the Yale School of Medicine from 1935 to 1940, was presented to Yale University Dec. 11. Dr. and Mrs. Bayne-Jones were present at the ceremony in the Historical Library of the School of Medicine when the portrait was unveiled. The portrait is a gift of colleagues, friends, and former students.

Dedicate Hospital.—Dedication of the 50-bed Grover F. Powers Hospital at the Connecticut State Health Department's Southbury Training School took place Nov. 15. This hospital, to which a new wing has recently been added, honors Dr. Grover F. Powers, department of pediatrics, Yale University School of Medicine, New Haven, for 25 years as a member of the board of trustees of Southbury Training School since its founding in 1940. Dr. Powers was president of the American Pediatric Society in 1947 and received the Howland Award in 1953. He has served on advisory committees of the U. S. Children's Bureau and since 1952 has been chairman of the Scientific Research Advisory Board of the National Association for Retarded Children. Dr. Powers retired at Yale in 1952.

Grover F. Powers Hospital, Southbury Training School

DISTRICT OF COLUMBIA

Research Program for High School Students.—Georgetown University will inaugurate a new research program this summer designed to point a way "to help meet the threatened shortage of physicians and dentists," the Very Reverend Edward B. Bunn, S.J., president of the university, announced. It will provide an opportunity for 20 boys and girls from district and metropolitan area high schools, public and private, to do research work in the Schools of Medicine and Dentistry at

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

the Georgetown Medical Center and prepare for careers in medical and dental science. Students will participate as members of various teams actively engaged in research in some basic or clinical science. The teams will generally include, in addition to the high school student and faculty investigators, a medical or dental student research fellow. Weekly seminars will be held during the entire summer period, at which the research teams will report to the group on their activities. Students selected for the program will receive an award of $100. The university will provide the necessary facilities, supplies, and equipment. High school juniors will be eligible to apply. Application forms can be obtained from the Registrar, Georgetown University Schools of Medicine and Dentistry. Any student in a college preparatory course, regardless of his major field of interest, is eligible. Candidates must provide a letter of reference from a high school science or mathematics teacher and another from a social science, art, history, language, or English teacher. Applications will be reviewed by a committee at the medical center and selected applicants will be interviewed. Application forms and reference letters must be submitted by Feb. 15. Applicants will be notified of their selection or rejection by April 1.

FLORIDA

Heart Program in Orlando.—The Orange County Heart Association will present a program, "Advances in Cardiovascular Disease," at the Cherry Plaza Hotel, Orlando, Feb. 6, 9 a. m. Guest speakers will be Dr. Andrew G. Morrow, of the National Heart Institute, Bethesda, Md.; Dr. Charles K. Friedberg, of Mt. Sinai Hospital, New York City; Dr. Harriet P. Dustan, of the Cleveland Clinic; and Dr. Philip Samet, of Mt. Sinai Hospital, Miami Beach. There will be a morning and afternoon session. All physicians are invited. Information may be obtained from Mrs. Emma Britt, Orange County Heart Association, 2904 N. Orange Ave., Orlando, Fla.

HAWAII

Health Statistics.—The 1958 annual report for the Department of Health, Territory of Hawaii, was recently published. The estimated civilian population for Hawaii for Jan. 1, 1959, was 585,025, of which 449,910 live in the county of Honolulu. In 1950 the total population was 499,794. Life expectancy at birth in the territory for 1949-1951 was 67.76 years for males and 71.29 years for females, as compared with 65.47 and 70.96 for the United States, respectively. The number of live births during 1958 was 16,710 and the number of deaths 3,072, giving a birth rate of 29.0 per 1,000 persons and a death rate of 5.4. Of the total number of births, 99.0% occurred in a hospital; 0.1% were delivered by midwives. The total of illegitimate births during the year was 812, a rate of 48.5 per 1,000 live births. The highest number of illegitimate births, 247, was among women in the 20-24 age group. Of the total births, 8,653 were male and 8,057 were female. The 10 leading causes of death for 1958 were as follows: (1) diseases of the heart; (2) cancer and other malignant neoplasms; (3) diseases of early infancy; (4) cerebral hemorrhage; (5) accidents (all forms); (6) influenza and pneumonia; (7) congenital malformations; (8) diabetes mellitus; (9) suicide; (10) nephritis and nephrosis. In 1933 the 10 leading causes of death included tuberculosis (3rd); diarrhea and enteritis (9th); and Hansen's disease (10th). Reporting on hospitalization under the medical care program for the territory, the Department of Health stated that the total cost of the program was $820,381.05, of which $313,223.18 was for the medically indigent. The number of days of patient hospital care for 1955 was 49,990 and the cost per patient day was $16.67. In 1958 the number of patient days was 35,408 and the cost per patient day was $22.77.

IOWA

Plan Two Structures for Psychopathic Hospital.—Preliminary budgets for constructing and equipping two structures at the State University of Iowa's Psychopathic Hospital were approved by the State Board of Regents. Funds for the structures, a research addition to the present building and a separate but connected unit for emotionally disturbed children, will come from state appropriations augmented by U. S. Public Health Service grants. The 58th General Assembly appropriated $235,000 for the research wing, with the federal government contributing a like amount. For the emotionally disturbed children's unit, the state appropriated $170,000, to which the U. S. Public Health Service added $85,000. Dr. Paul E. Huston, head of psychiatry at SUI and director of the Psychopathic Hospital, said, the ground floor of the addition will contain an observation laboratory, an epidemiological statistical center, a psychoneurophysiological laboratory, four sound-proof laboratories, an electronics and equipment shop, and two staff offices. The first floor will contain six staff offices, two office-laboratories, a section for experimental animal work, and six laboratories for the study of human behavior, alcoholism, and biochemical factors in mental disorders. The emotionally disturbed children's unit will be located north of the research addition and connected to it by a corridor. The ground floor of the three-floor building will contain a mechanical equipment room, a storage room, a library, four offices, a play room, and six rooms for examinations, interviews, and observations. The first floor will consist of reception room, two offices, a visitors' waiting room, a classroom, and living, feeding, and kitchen area. The second floor will contain a nurses' station and a utility room, with the remaining rooms devoted to sleeping rooms and patient rooms to accommodate about 27 children.

MASSACHUSETTS

Annual Tufts Alumni Lecture.—Capt. Roger H. Fuller, M.C., U. S. Navy, will give the annual Tufts Medical Alumni Lecture on Tuesday, Feb. 2, 11 a. m., at Tufts University Medical School, 136 Harrison Ave., Boston. His subject will be "Activities of the Armed Forces Institute of Pathology." Dr. Fuller, a graduate of Tufts Medical School in 1938, is deputy director of the Armed Forces Institute of Pathology, Washington, D. C. All students and physicians are invited.

MICHIGAN

Expand Public Health Teaching Facilities.—A newly opened 1½-million-dollar addition to the University of Michigan School of Public Health has doubled the teaching and research facilities of the unit, one of 10 accredited public health schools in the United States. The addition consists of two four-story wings attached to the original building which was erected in 1943. The wings include laboratories for research in epidemiology, industrial health, radiological health, and sanitation. There are multipurpose lecture and workshop rooms, specially constructed radiation labs with lead-lined walls, library facilities, and a two-story open laboratory for testing large equipment. Additional space has been provided for each of the school's five departments: environmental health, epidemiology, industrial health, public health practice, and public health statistics. The school also houses the National Sanitation Foundation. The new structure houses over a quarter-million dollars worth of research equipment. The building was erected with funds from the U. S. Public Health Service and the W. K. Kellogg Foundation.

NEW YORK

Dr. Preston Named Physiology Chairman.—Dr. James B. Preston was appointed professor and chairman of the department of physiology at the Upstate Medical Center, State University of New York College of Medicine, Syracuse, effective July 1. Dr. Preston will succeed Dr. Gordon K. Moe, who leaves in June to become laboratory director of the Masonic Foundation for Medical Research and Human Welfare, in Utica. Dr. Preston was formerly assistant professor of physiology. He came to the medical center in July, 1956, as instructor in physiology.

Personal.—New York Health Department's Office of Personnel announced the permanent field appointment of Dr. William G. Hafner Jr., Weedsport, as assistant district health officer in the Syracuse District Office. The appointment became effective Nov. 4.——Dr. Vivian A. Van Volkenburgh, Albany, retired as assistant commissioner for local health services with the New York State Health Department, effective Jan. 1, Dr. Van Volkenburgh has been associated with the State Health Department since 1935.

New York City

Home for Jewish Cancer Patients.—On Dec. 14 Beth Abraham Home, Allerton Avenue at Bronx River Parkway, began admitting Jewish persons with terminal cancer for care. The new service will enable 25 patients to live in an orthodox environment and benefit from medical and nursing services maintained by Beth Abraham. The number of beds allocated to this program—5% of the home's 531-bed capacity—may be increased, Mrs. Samuel Zahn, president of the nonprofit home, said. The social service department of the home will process applications for admission. Beth Abraham Home is affiliated with and receives its major philanthropic support from the Federation of Jewish Philanthropes of New York.

Personal.—Dr. George E. Palade, professor at the Rockefeller Institute, delivered the annual Research Society Lecture at the State University of New York Downstate Medical Center, Brooklyn, Dec. 14, presenting "Structure and Function in Blood Capillaries." Dr. Palade received his M.D. degree from the University of Bucharest, Rumania, and was an associate professor at the medical school there.——Dr. Robert Turell, invited to present papers before the ninth congress of the Sociedade Brasileira de Proctologia on Nov. 5 and 7 in Porto Alegre (Brazil) was given honorary membership in that society. He also presented a paper before proctologic and surgical groups in Montevideo, Uruguay, Buenos Aires, Argentina, and in Rio de Janeiro.

TEXAS

Dr. Cooke Honored.—Dr. Willard R. Cooke's portrait became the 21st to be hung in the gallery of Texas medical men at the library of the University of Texas Medical Branch, Galveston. More than 3,000 doctors were trained under Dr. Cooke's tutelage. When he retired as professor emeritus in September, after 35 years of teaching, he was chairman of the school's obstetrics and gynecology department. Dr. John D. Weaver, of Austin, president of the eight-year old Willard Cooke Club, spoke for the group at the presentation.

GENERAL

Intermountain Pediatric Meeting.—The Intermountain Pediatric Society will hold its annual clinical convention at the Stardust Hotel, Las Vegas, Nev., March 28 and 29. The program will be presented by the following physicians: Dr. Robert E. Cooke, Baltimore; Dr. Louis K. Diamond, Boston; and Dr. Frederic N. Silverman, Cincinnati. Sessions will extend from 10 a. m. to 2 p. m. daily, including a round-table luncheon. For information, write the Intermountain Pediatric Society, 2000 S. 9th East, Salt Lake City, Utah.

Grants to Support Clinical Pharmacology.—The Burroughs Wellcome Fund, a nonprofit organization with headquarters in Tuckahoe, N. Y., announced through its president a program of grants to medical schools to maintain new faculty positions in clinical pharmacology. During the next five years, the fund will award five grants to medical schools to underwrite the salary of a full-time teacher in clinical pharmacology. Each of these grants will be a total of $75,000 payable over a five-year period. The grants will be known as the Burroughs Wellcome Fund Clinical Pharmacology Grants. One reason for setting up the grants is the "shortage of qualified physician investigators specializing in clinical pharmacology."

Award for Cancer Research.—The Ann Langer Cancer Research Foundation announced the third annual award of $500 for "meritorious investigation in the field of cancer research, either clinical or laboratory." The award is being supported by the family of the late Bertha Goldblatt Teplitz and carries her name. Competition is limited to physicians and other scientists, clinical or laboratory, under the age of 45. The name of the recipient of the 1960 award will be announced May 1. Nominations should be submitted to the Teplitz Award Committee, 612 N. Michigan Ave., Chicago 11, no later than Feb. 1, and should be accompanied by a short one-page statement and biography.

Lung Cancer Study.—The American Cancer Society reported that a long-term study indicates that the incidence of lung cancer is twice as great among middle-aged men as tuberculosis is. The results of the study were reported Dec. 29 by the society, which helps support the research by Drs. Katharine R. Boucot and David A. Cooper, of the Philadelphia Pulmonary Neoplasm Research Project. The Philadelphia Tuberculosis and Health Association cooperates with the Cancer Society in the project, which is endorsed by the Philadelphia Medical Society. Six years ago 6,137 men over 45 agreed to have annual or semiannual chest x-rays and to answer questions about symptoms of lung disease. During an average period of six years, 31 men developed lung cancer. Over the same period 16 men developed tuberculosis, and an additional eight former tuberculosis patients showed reactivation of the disease.

Surgical Journal Has Anniversary.—Seventy-five years of continuous publication was celebrated by *Annals of Surgery* with the publication of its December issue. Reportedly the oldest surgical journal in any language in the world, *Annals of Surgery* was founded by Lewis Stephen Pilcher, who remained editor for 50 years. The publisher from 1885 to 1892 was J. H. Chambers, of St. Louis; from 1892 to 1897 it was published by the University of Pennsylvania, and in 1897 J. B. Lippincott Company took over the copyright. The journal is the official organ of the American Surgical Association, the Southern Surgical Association, the New York Surgical Society, and the Philadelphia Academy of Surgery. The present editorial and advisory board is headed by Dr. John H. Mulholland, of New York City.

Gastroenterology Meeting in New Orleans.—The 10th semiannual meeting of the Gastroenterology Research Group will be held at the Roosevelt Hotel, New Orleans, Thursday, March 31 at 2 p. m. A symposium, "The Genetic Approach to the Study of Gastrointestinal Disease," will be moderated by Dr. Victor A. McKusick, Baltimore. Papers to be given under the general topics of liver, pancreas, and stomach and intestine are as follows:

The Hereditary Hyperbilirubinemias, Dr. Barton Childs, Baltimore.
Hemochromatosis, Prof. Maurice Lamy, Paris.
Cystic Fibrosis of the Pancreas, Arthur G. Steinberg, Ph.D., Cleveland.
Polyposis, Thomas E. Reed Jr., Ph.D., Ann Arbor, Mich.
Pyloric Stenosis, Dr. Brian MacMahon, Boston.
Duodenal Ulcer, Dr. David Price-Evans, Liverpool, England.

For information, write Dr. Nicholas C. Hightower Jr., Scott and White Memorial Hospital, Temple, Texas, Secretary-Treasurer.

Project to Standardize Transfusion Equipment.—Work is progressing on an international project to make component parts of blood transfusion equipment interchangeable. The standardization work for blood transfusion equipment is conducted by Technical Committee 76 of the International Organization for Standardization. The committee held its second meeting in London, England, in September. The aim of the committee is to achieve functional interchangeability between transfusion equipment used in different countries by specifying essential requirements but not details of design. A draft proposal for standards for disposable (single-use) equipment was discussed at the London meeting. Arrangements were made for extensive practical trials on the interchangeability of equipment at present in use in the member countries. A new working group was set up at the London meeting to study the requirements for interchangeability, proper functioning, and safety of plastic containers for blood. The United States holds the secretariat of of this group. American interests in international standards work are represented through the American Standards Association, U. S. A. member of ISO.

Society News.—The Tennessee Valley Medical Assembly will be held in Chattanooga, Tenn., Sept. 26-27, and the officers elected for this meeting are: Drs. George K. Henshall Jr., president; Augustus McCravey, president-elect; Charles W. Hawkins, secretary-treasurer; Robert A. Waters, chairman; John E. Strickland Jr., co-chairman; and William G. Stephenson, founder.——Brig. Gen. Joseph J. Foss, Sioux Falls, S. D., former governor of South Dakota, is the new president of the **National Society for Crippled Children and Adults,** the Easter Seal Society. He was elected Dec. 1.——Dr. Henning M. Berg, Bismarck, N. D., was named president-elect of the **Radiological Society of North America** at the society's 45th annual meeting Nov. 16-20. Dr. Laurence L. Robbins, Boston, was retiring president. Other chief officers named include Dr. Theodore J. Wachowski, Auroa, Ill., president; Dr. Charles M. Gray, Tampa, Fla., chairman of the board of directors; Dr. Donald S. Childs, Syracuse, N. Y., secretary-treasurer; and Dr. Robert D. Moreton, Fort Worth, Texas, new member of the board of directors. The society's 1960 annual meeting will be held in Cincinnati Dec. 4-9 at the Netherland Hilton Hotel.

Heart Association Begins Direct Publication of Journals.—The American Heart Association began direct publication of its two scientific journals, *Circulation* and *Circulation Research* with the January, 1960, issues. The journals were previously published by a private publishing firm. Under the new management, *Circulation* will regularly feature symposium subjects relating to cardiovascular diseases. The first symposium, congestive heart failure, will be carried in the January, February, and March, 1960, issues. As in the past, other sections of *Circulation* will be devoted to original articles and reviews, abstracts of international contributions to cardiologic problems, book reviews, and news notices of particular interest to clinicians and cardiologists. Issued monthly by the association since 1950, *Circulation* is edited by Dr. Herrman L. Blumgart, of Boston, professor of medicine, Harvard University. *Circulation Research* is devoted exclusively to reports on fundamental research studies as they apply to cardiovascular medicine and surgery. Inaugurated by the association in 1953, the journal is issued bimonthly and edited by Dr. Carl F. Schmidt, of Philadelphia, professor of pharmacology, University of Pennsylvania Medical School.

Meeting of Allergists in Florida.—The 16th annual meeting of the American Academy of Allergy will be held Jan. 11-13 at the Hollywood Beach Hotel in Hollywood-by-the-Sea, Fla. Thirty-one scientific papers will be presented. A postgraduate course under the direction of the academy's Committee on Postgraduate Education will be conducted on Jan. 9 and 10. Physicians, guests, residents, and interns are invited to attend all of the scientific sessions. Advance registration for the postgraduate course is required. The scientific program will feature four scientific addresses: Dr. Robert A. Cooke, director, Institute of Allergy, Roosevelt Hospital, New York City, will present the First William H. Schultz Lectureship during the evening session, Jan. 11; Dr. Byron H. Waksman, assistant professor of bacteriology and immunology, Harvard Medical School, Boston, will present a report, "Delayed Hypersensitive Reactions: A Growing Class of Immunologic Phenomena"; Dr. David V. Bates, associate professor of medicine, McGill University, Montreal, Canada, will discuss "The Consequences of Structural and Functional Obstruction to Air Flow in the Lung" on Jan. 12; and Rupert E. Billingham, D.Sc., Wistar Professor of Zoology, University of Pennsylvania, Philadelphia, will present "Some Aspects of Tissue Transplantation Immunity" the evening of Jan. 12. The annual business meeting and election of officers will be held at 4 p. m., Jan. 12. Nine scientific exhibits and 49 exhibits by commercial firms will be displayed. For information, write the Academy's Executive Office, 756 N. Milwaukee St., Milwaukee 2, Wis.

Report on Births.—Statisticians of the Metropolitan Life Insurance Company reported that births in recent years have broken all previous records in the United States and Canada, and in Australia and New Zealand as well. In all four countries, the birth rate in the last decade has been about one-third greater than that recorded just prior to World War II. In the U. S., births have numbered well over 4 million in each of the past five years; for the period of 1947-1958 the total exceeded 47 million. Many European countries have had declining birth rates since the postwar high, although several have halted and reversed the downward trend. Finland experienced a sharper decrease than any other country in Europe; the rate there fell one-third, from 28.0 per 1,000 population in 1947 to 18.5 in 1958. Over the same period Sweden, Denmark, the Netherlands, and Czechoslovakia recorded reductions of about one-quarter. More moderate declines of about one-sixth were recorded in France and Norway. England and Wales have experienced rising birth rates in recent years. After falling from 20.5 per 1,000 in 1947 to 15.0 in 1955, the rate rose to 16.4 in 1958—higher than the 15.1 rate for 1938, the last prewar year. Scotland shows a similar trend. West Germany also has shown a rising birth rate recently, but East Germany has shown a continuing decline. Japan reduced its birth rate by about one-half between 1947 and 1958—from 34.3 per 1,000 population in 1947 to 17.2 in 1957 and 18.0 in 1958. Figures released by the Soviet Union indicate that the birth rate is not appreciably different from that in the United States, even though the number of births there is greater because of the larger population. No reliable figures are available for India or for the mainland of China, which is believed to have a population exceeding 650 million.

Mental Health Year.—World Mental Health Year will be proclaimed for 1960 in a project designed to give the impetus to advances in mental health around the globe that the International Geophysical Year attained for the physical sciences. The year will be inaugurated on Jan. 15 by the Academy of Religion and Mental Health and the World Federation for Mental Health as the highlight of the academy's first annual meeting, which will take place Jan. 14-15 at the Hotel Biltmore, New York City. The year will be climaxed by an International Congress on Mental Health, to be held in Paris in August, 1961, at which reports on the progress of the significant effort will be presented. The Academy of Religion and Mental Health, co-sponsor of the year, is a national nonprofit educational and research organization "devoted to betterment of man's spiritual and emotional health through integration of the moral values of religion and the scientific insights of psychiatry and the behavioral sciences." The chairman of the annual meeting will be Dr. Francis J. Braceland, chief psychiatrist at the Institute in Living in Hartford, Conn., and a past-president of the American Psychiatric Association. The address of welcome will be given by Dr. Harvey J. Tompkins, president of the academy, who is director of the psychiatric division of St. Vincent's Hospital, New York City. The morning and afternoon sessions of the two days will be devoted to workshops, panels and seminars on subjects involving education, theology, psychiatry, and their interrelationships. The World Federation for Mental Health, which originally proposed World Mental Health Year, was founded in 1948 at the third International Congress on Mental Health. It has working relations with the United Nations, official status as a consultant of the Economic and Social Council, the World Health Organization, the United Nations Educational, Scientific, and Cultural Organization, and the United Nations Children's Fund.

FOREIGN

Czechoslovakian Physicians Sentenced.—The Austrian Physicians Newspaper of Nov. 10 reported that the district court in Prague on Oct. 20, after a session of several days, sentenced a group of 36 physicians and employees of the Public Health Department to stay in prison for periods of more than 130 years. The defendants were accused of having healthy persons reported as sick or invalids, or of having helped patients to get unjustified compensation with the aid of forged papers. These sentences are related to the opposition of the physicians to the total socialization of the Health Service which since the start of 1959 has no longer permitted private offices.

Meeting on Social Work in Rome.—"Social Work—Its Function and Responsibilities in a Changing World" will be the theme of the 10th International Conference of Social Work to be held in Rome, Italy, Jan. 8-14, 1961. Dr. George F. Davidson, Canadian Deputy Minister of National Welfare, is president of the conference. The international conference is a permanent world-wide organization which in its biennial meetings brings together agencies and individuals concerned with meeting the social welfare needs of people. Its major purpose is to provide a forum for the discussion of social welfare and related issues. The ISSW is an independent organization, nongovernmental, nonpolitical, and nonsectarian, and was established in 1928. Any interested person is welcome to attend. The secretariat of the ICSW is at 345 E. 46th St., New York City, with regional offices in Paris and Bombay. Mr. Joe R. Hoffer is secretary general of the organization.

Congress on Alcoholism in Stockholm.—The 26th annual Congress on Alcohol and Alcoholism will be held July 21-Aug. 5 in Stockholm, Sweden, under the high patronage of His Majesty King Gustav VI Adolf. The congress is divided in sections of five main themes, one plenary session and daily separate sessions, as follows:

A. Alcohol and the Community
  1. Alcohol consumption and legislation on alcohol in different countries.
  2. Alcohol problems in industry and road traffic
  3. Treatment of alcoholism
  4. Education, preventive work, contribution of voluntary organizations including the activities of temperance associations.

B. Research Problems
  5. Aspects and results of medical and sociological alcohol research (in cooperation with the Committee for Alcohol Research of the Swedish Medical Research Council).

The congress is open to delegates from governments, public authorities and institutions, research workers, and others interested in the program to be discussed. Registration should be sent not later than May 1 to the Twenty-Sixth International Congress on Alcohol and Alcoholism, Karlavagen 58, Stockholm 5, Sweden. Congress fee is 75 Swedish crowns (15 U. S. dollars). Papers to be read at the congress should reach the secretary not later than March 1.

International Conference on Mental Deficiency.—As a contribution to World Mental Health Year, 1960, the American Association on Mental Deficiency has initiated plans for a second International Conference on Mental Deficiency in cooperation with the Royal Medico-Psychological Association and the British Psychological Association. This conference is known as the "London Conference on Scientific Aspects of Mental Deficiency." The London Conference will deal with the "latest medical, psychological, social, educational and administrative developments" in mental deficiency. It is open to professional workers. Meetings will be held in London during July 24 to 29, 1960, and will precede the meetings of the World Federation for Mental Health to be held in Edinburgh Aug. 7-12. For information, write Mr. Harvey A. Stevens, Chairman, AAMD Committee on International Conference on Mental Deficiency, 301 Troy Dr., Madison 4, Wis.

CORRECTION

Medicine at Work.—The article "This Trouble Shooting Clinic Is Strengthening a Community," in The Journal, Nov. 21, page 1697, should have stated that the idea of the Trouble Shooting Clinic originated with Dr. Leopold Bellak.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 19-20. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination*. Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Connecticut:* *Regular. Examination*. Hartford, Mar. 8-10. Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven. *Homeopathic. Examination*. Derby, Mar. 8. Sec., Dr. Ronald A. Davis, 38 Elizabeth St., Dover.

Delaware: *Examination*. Dover, Jan. 12-14. *Endorsement*. Dover, Jan. 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Georgia: *Examination and Reciprocity*. Atlanta, June. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call*. Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Examination*. Honolulu, Jan. 11-12. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination* and *Reciprocity*. Boise, Jan. 11, 12, 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Indiana: *Examination*. Indianapolis, June 1960. *Reciprocity*. Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:* *Examination and Reciprocity*. Kansas City, Jan. 15-16. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Massachusetts: *Examination*. Boston, Jan. 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston.

Minnesota:* *Examination*. Minneapolis, Jan. 19-21. *Reciprocity*. Minneapolis, Jan. 21. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

Mississippi: *Examination*. Jackson, June. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

Montana: *Examination and Reciprocity*. Helena, April 5. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination*. *Omaha, June 13-15, 1960*. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

New Hampshire: *Examination*. Concord, March 9-11. *Reciprocity*. Concord, March 9. Sec., Dr. Edward W. Colby, 61 South State St., Concord.

New Jersey: *Examination*. Jan. 19-22. *Reciprocity*. Monthly, Admin. Sec., Michael E. H. Sweeney, 28 West State St., Trenton.

Oklahoma:* *Examination*. Oklahoma City, May 31-June 1. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Oregon:**Examination*. Portland, Jan. 12-13. *Reciprocity*. Portland, Jan. 14-16. Ex. Sec., Mr. Howard J. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination*. Philadelphia, January. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

South Dakota:* *Examination*. Sioux Falls, Jan. 19-20. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Utah: *Examination*. Salt Lake City, July 6-8. Director, Mr. Frank E. Lees, 324 *State Office Bldg., Salt Lake City* 1.

Washington:* *Examination*. Seattle, Jan. 11-13. Administrator, Professional Division, Capitol Bldg., Olympia.

West Virginia: *Examination*. Charleston, Jan. 11-13. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Examination*. Madison, Jan. 14-16. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Building, 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity*. Cheyenne, Feb. 1. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arkansas: *Examination*. Little Rock, April 21-22. Sec., Dr. A. W. Ford, Department of Education, Education Bldg., Little Rock.

Colorado: *Examination and Reciprocity*. Denver, March 2-3. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination*. New Haven, Feb. 13. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

Iowa: *Examination*. Des Moines, Jan. 12. *Reciprocity*. Des Moines, Jan. 11. Sec., Dr. Elmer W. Hertel, Waverly.

Kansas: *Examination*. Kansas City, June 10-12. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

Michigan: *Examination*. Detroit and Ann Arbor, Feb. 12-13. Sec., Mrs. Anne Baker, West Michigan Ave., *116* Stevens T. Mason Bldg., Lansing.

New Mexico: *Examination*. Santa Fe, Jan. 17. *Reciprocity*. Santa Fe, Jan. 9. Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

Oklahoma: *Examination*. Oklahoma City, April 15-16. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Texas: *Examination*. Austin, Houston, Galveston and possibly Dallas, April 15-16. Sec., Dr. Cornelia M. Smith, State Office Bldg., 201 East 14th St., Austin.

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*Basic Science Certificate required.

DEATHS

Coleman, John Alexander Ⓜ Plant City, Fla.; Tulane University School of Medicine, New Orleans, 1924; interned at the Medical College of Virginia Hospital Division, Richmond; surgeon for the Seaboard Air Line Railway since 1929; member of the county school board; president of the Plant City Music Association; organizer of the Elks Lodge; in 1956 he was selected as the most outstanding citizen of Plant City; on the staff of the South Florida Baptist Hospital; died Oct. 19, aged 63.

Connell, William Francis Ⓜ Pittston, Pa.; Georgetown University School of Medicine, Washington, D. C., 1933; interned at the Wilkes-Barre (Pa.) General Hospital; served with the Army Medical Corps during World War II, receiving the Purple Heart and the Bronze Star; on the staff of Pittston Hospital; died in Mercy Hospital, Scranton, Oct. 18, aged 55.

D'Elia, Vincent Anthony Louis Ⓜ Quincy, Mass.; Tufts University School of Medicine, Boston, 1937; interned at the Quincy City Hospital, where he also served a residency; died Oct. 6, aged 48.

Durrah, Fred Falls Ⓜ Plainfield, N. J.; Howard University College of Medicine, Washington, D. C., 1913; for many years a director of the Representative Building and Loan Association; a founder of the National Association for the Advancement of Colored People; member of the Plainfield Chamber of Commerce; served in the Baby Keep Well Station and on the staff of Muhlenburg Hospital; died Oct. 8, aged 76.

Erlanger, Herman Ⓜ St. Louis; Washington University School of Medicine, St. Louis, 1937; interned at the Boston City Hospital; served residencies at the Peter Bent Brigham Hospital, Boston, and the University Hospital, Ann Arbor, Mich.; certified by the National Board of Medical Examiners in 1941; served during World War II with the Army Medical Corps; assistant professor of medicine and preventive medicine at his alma mater; director of health service at Barnes Hospital, where he died Oct. 14, aged 47.

Finnigan, Frank Roman Ⓜ St. Louis; St. Louis University School of Medicine, 1920; interned at St. Luke's Hospital, St. Louis; specialist certified by the American Board of Internal Medicine; member of the American College of Physicians and the Catholic Physicians' Guild; member of a group which organized the Soper-Mills Clinic in 1928; headed the staff of De Paul Hospital from 1941 to 1944; on the staffs of St. Mary's and St. Louis City hospital; died in De Paul Hospital Oct. 10, aged 65.

Flanagan, William Latane Ⓜ Christiansburg, Va.; Medical College of Virginia, Richmond, 1953; interned at the Naval Hospital, Charleston, S. C.; died in the Radford (Va.) Community Hospital Oct. 11, aged 31.

Foreman, Thomas Frederick Ⓜ Syracuse, N. Y.; born in Syracuse Oct. 3, 1876; State University of New York College of Medicine, Syracuse, 1900; veteran of World War I; for many years a deputy health commissioner; for many years on the staff of the City Hospital; on the staff of the Syracuse Memorial Hospital; died Oct. 12, aged 83.

Harris, Dallas Dale Ⓜ Marshalltown, Iowa; State University of Iowa College of Medicine, Iowa City, 1940; interned at Brooklyn (N. Y.) Methodist Hospital; served in the medical corps of the U. S. Navy during World War II; past-president of the Marshall County Medical Society; trustee on the board of the Iowa State Obstetrical Society; formerly chief of staff of the Evangelical Hospital and the Mercy Hospital; died Oct. 18, aged 42.

Harris, Richard August Ⓜ Quincy, Ill.; University of Illinois College of Medicine, Chicago, 1924; interned at Grant Hospital, Chicago; served during World War I; member of the American Society of Anesthesiologists and the International Anesthesia Research Society; formerly editor of the *Quincy Medical Bulletin;* died Oct. 6, aged 61.

Harwell, David F. Ⓜ Jacksonville, Fla.; Atlanta (Ga.) College of Physicians and Surgeons, 1907; died Oct. 7, aged 81.

Huff, Charles Frederick Ⓜ Sturgeon Bay, Wis.; born in Burchard, Neb., Jan. 25, 1877; Northwestern University Medical School, Chicago, 1908; interned at St. Luke's Hospital, Chicago; served during World War I; during World War II he served as a member of the Selective Service Area Appeals Board; at one time practiced in Memphis, Tenn.; for many years a surgeon with the U. S. Public Health Service; city health officer for 30 years; served as president of the board of education; president of the Sturgeon Bay Savings and Loan Association; died Oct. 7, aged 82.

Jackemy, Edward Joseph Ⓜ Los Gatos, Calif.; University of California School of Medicine, Berkeley–San Francisco, 1932; interned at Highland–Alameda

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Ⓜ Indicates Member of the American Medical Association.

County Hospital, Oakland; served with the Army Medical Corps during World War II; member of the Industrial Medical Association; died Oct. 12, aged 53.

Jevrem, Dragoljub S. Ⓜ Canton, Ohio; Universite de Paris Faculte de Medecine, 1923; served with the Yugoslavian Army during World Wars I and II; for 10 years a member of the Royal Yugoslav Parliament; on the staffs of Aultman, Mercy, and Timken Mercy Hospitals; died Oct. 21, aged 63.

Kalichman, Hirsh George, Santa Monica, Calif.; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, 1908; died Oct. 9, aged 80.

Kerr, Isabelle Dickieson, Boston; Tufts University School of Medicine, 1903; did postgraduate work at the University of Edinburgh Medical School, Scotland, and the Nose and Throat Clinic, Vienna, Austria; specialist certified by the American Board of Otolaryngology; member of the New England Oto-Laryngological Society and the American Women's Medical Association; on the staffs of the Massachusetts Eye and Ear Infirmary, Massachusetts General Hospital, and the New England Hospital, where she was a consultant; died in Watertown, Mass., Oct. 12, aged 78.

Langum, Ival Goodver H., St. Charles, Ill.; born in Eau Claire, Wis., Feb. 18, 1877; National Medical University, Chicago, 1904; served during World War I; for many years mayor of St. Charles; on the staffs of Community Hospital, Geneva, and Delnor Hospital; died Oct. 27, aged 82.

Lanning, Nicholas E. Ⓜ Grand Rapids, Mich.; Rush Medical College, Chicago, 1935; interned at Harper Hospital, Detroit; member of the American Academy of General Practice; died Oct. 17, aged 52.

Long, William F., Mertztown, Pa.; Jefferson Medical College of Philadelphia, 1902; for a time practiced in Bowmansville, Pa.; died Oct. 20, aged 86.

Ludwig, Oscar Dennen Ⓜ Indianapolis; born at Williamston, Mich., Oct. 1, 1880; Indiana University School of Medicine, Bloomington-Indianapolis, 1910; served during World War I; member of the American Academy of General Practice; health officer of Marion County; on the staffs of St. Francis and Methodist hospitals; died in Riverside Hospital, Noblesville, Oct. 13, aged 79.

Marcus, David Ⓜ Tucson, Ariz.; McGill University Faculty of Medicine, Montreal, 1923; interned at Manhattan State Hospital, New York City, and Mt. Sinai Hospital, Cleveland; during World War II served as a major at Fitzsimons General Hospital, Denver; member of the American College of Chest Physicians and the American Trudeau Society; on the staff of Tucson Medical Center; died Oct. 8, aged 58.

Martin, John Gregory Ⓜ Wadsworth, Ohio; born in India in 1890; Western Reserve University School of Medicine, Cleveland, 1916; at one time practiced in Clinton; veteran of World War I; fellow of the American College of Surgeons; a missionary in India and Pakistan, he was instrumental in the construction of a hospital at Taxila, Pakistan; on the staffs of Akron (Ohio) Children's Hospital and Wadsworth Municipal Hospital, where he was formerly chief of staff and where he died Oct. 12, aged 69.

McDede, Joseph Searle Jr. Ⓜ Fort Benton, Mont.; Columbia University College of Physicians and Surgeons, New York City, 1937; for a time practiced in Winoma, W. Va.; during World War II served in the India-China-Burma Theater as a flight surgeon; died Oct. 16, aged 49.

McDonald, Thomas Alexander Ⓜ Monroe, Mich.; University of Toronto Faculty of Medicine, 1924; interned at the Charleston (W. Va.) General Hospital and Training School; served a residency at Grace Hospital, Detroit; served with the Canadian Army and the Royal Air Force during World War I; fellow of the American College of Surgeons; for many years a member of the House of Delegates of the Michigan State Medical Society; past-president of the Monroe Rotary Club; formerly was chief of staff of Mercy Hospital; died Oct. 13, aged 65.

Mehaffey, Jonathan William Ⓜ Birmingham, Ala.; Birmingham Medical College, 1913; member of the Alabama Academy of General Practice and the American Academy of General Practice; died Oct. 16, aged 72.

Morrow, Milton, Muskogee, Okla.; born in Murray, Neb., Dec. 30, 1874; Lincoln (Neb.) Medical College, Eclectic, 1898; for several years professor of materia medica at his alma mater; for many years practiced in Seward, Neb.; later practiced in Great Bend, Kan., where he was appointed eye, ear, nose, and throat specialist of the Western Kansas Crippled Children Association, and where he was on the staff of the St. Rose Hospital; died Oct. 14, aged 84.

Nagle, Clyde Leo Ⓜ Elmira Heights, N. Y.; University of Buffalo School of Medicine, 1943; interned at the Arnot Ogden Memorial Hospital, where he interned, served a residency, and was chief obstetrician and instructor of obstetrics and gynecology in the School of Nursing; director of the Chemung County Community Chest; past-president of the county chapter of the American Cancer Society; member of the Child and Family Service board of directors and the school board; guest lecturer at Corning Community College; senior physician in the department of correction, Elmira Reception Center; president of the medical staff of Arnot Ogden Hospital and on the staff of St. Joseph's Hospital; died Oct. 7, aged 43.

Nee, Francis, Spring Green, Wis.; born in Richland County, Nov. 18, 1879; University of Illinois College of Medicine, Chicago, 1906; served on the school board and was a director of the State Bank of Spring Green; was honored at the Spring Green centennial in 1957 for fifty years of medical service to the community; died in Dodgeville Oct. 9, aged 79.

Palmer, Edwin Obadiah Ⓜ Los Angeles; born in Schenectady, N. Y., June 17, 1872; Columbia University College of Physicians and Surgeons, New York City, 1896; formed the Hollywood Medical Group, of which he was president; served as assistant county health officer and later as city health officer for Hollywood; president of the Federal Building Company; organized the *Hollywood Citizen* newspaper in 1906; served as lecturer and member of the executive committee of St. Vincent's Hospital; president of Hollywood Hospital; died Oct. 19, aged 87.

Pear, Henry Robert Ⓜ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, 1932; interned at the Monmouth Memorial Hospital, Long Branch, N. J.; on the staffs of the Providence, Garfield Memorial, and Sibley Memorial hospitals, Washington, D. C.; died Oct. 13, aged 56.

Scherl, Sam A. Ⓜ New York City; Marquette University School of Medicine, Milwaukee; 1926; interned at St. Joseph's Hospital, Ashland, Wis.; member of the Bronx Chapter of the American Academy of General Practice and Phi Delta Epsilon; on the staff of Lebanon Hospital; died in Montefiore Hospital Oct. 24, aged 60.

Sharp, Winfield Kennedy, Jr. Ⓜ Nashville, Tenn.; Atlanta (Ga.) College of Physicians and Surgeons, 1913; specialist certified by the American Board of Preventive Medicine; director of the State Health Department's indigent hospitalization program; served with the U. S. Public Health Service as regional director in Washington, Richmond, and New Orleans; for two years health and safety director for the Tennessee Valley Authority; helped in the establishment of a civil defense program for the Georgia Health Department; died Oct. 18, aged 73.

Smith, Arthur Andrew Ⓜ Hastings, Neb.; born in Sparta, N. C., July 5, 1884; Rush Medical College, Chicago, 1912; interned at Lincoln (Neb.) Sanitarium and St. Mary's Hospital, Rochester, Minn.; at one time district medical inspector and chief medical officer for the Veterans Bureau in Seattle; served during World War I; past-president of the Adams County Medical Society; fellow of the American College of Surgeons; member of Nu Sigma Nu; formerly on the staffs of the Mary Lanning Memorial Hospital and the Hastings State Hospital; died Oct. 13, aged 75.

Smith, Dean Stanley Ⓜ La Crosse, Wis.; University of Illinois College of Medicine, Chicago, 1915; interned at the Illinois Charitable Eye and Ear Infirmary, Chicago; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Oto-Laryngology and the American College of Surgeons; received the first distinguished alumnus award presented by River Falls (Wis.) State College for "personal accomplishment, civic responsibility and contributions to community and country and interest to this college, and highest integrity in professional, public and personal relationships"; on the staff of St. Francis Hospital; died Oct. 10, aged 70.

Stinson, Walter Samuel Ⓜ Bay City, Mich.; University of Michigan Medical School, Ann Arbor, 1929; interned at Grace Hospital, Detroit; served a residency at the Henry Ford Hospital, Detroit; former councilor of the Michigan State Medical Society and several times a delegate to its conventions; past-president of the Bay City Medical Association; member of the American Academy of General Practice and Phi Chi fraternity; president of Allen Medical Building Corporation; on the staffs of Mercy and General hospitals; died Oct. 15, aged 58.

Stygall, James Henry Ⓜ Indianapolis; University of Buffalo School of Medicine, 1910; past-president of the American College of Chest Physicians; member of the American College of Physicians and the American Trudeau Society; director of the Indiana Tuberculosis Association; conducted tuberculosis clinics at the Madison County Tuberculosis Association Headquarters; served as director of nutrition for the Indianapolis public school system for many years; assistant professor of medicine at Indiana University School of Medicine; died Oct. 18, aged 72.

Switzer, Lars Waldorf Ⓜ Essexville, Mich.; University of Illinois College of Medicine, Chicago, 1927; interned at Augustana Hospital, Chicago; at one time director of the Benzie County Health Department; physician at the Chevrolet plant in Bay City; member of the Industrial Medical Association; died in Mercy Hospital, Bay City, Oct. 15, aged 58.

Thomas, Harold E., Gloucester, Va.; born in Columbus, Ohio, June 29, 1875; The Hahnemann Medical College and Hospital, Chicago, 1903; died in Riverside Hospital, Newport News, Oct. 6, aged 84.

FOREIGN LETTERS

GERMANY

Calculating the Years of Life Lost.—K. H. Weber (*Bundesgesundheitsblatt* 2:151, 1959) said that the usual procedure in arranging the common causes of death in order of their importance is to take the total number of deaths from each cause in a given period, to relate this to the total population, and to arrange the causes of death in order according to the death rates thus obtained. Such an arrangement does not give a true indication of the relative importance of the individual causes of death but only of their relative frequency. Since it is not a matter of indifference to human society whether a particular death occurs in the early or the late years of life, it is proposed to list cause of death on a basis of the number of years of life lost, from an arbitrary standard of a 75-year life span.

According to this method of reckoning, causes of infant mortality would appear high on the list with a percentage of 31.2. In 1956, with respect to years of life lost among males, accidents took first place with 14.6%. Heart disease came next with 11.2% and then malignant tumors with 10.2%. For females, on the other hand, after infant mortality, malignant tumors were first with 17.2%, then heart disease with 9.7%, and cerebral hemorrhage with 6.2%. Accidents came far behind with 3.7%. Whereas by the traditional method of analysis mortality from tumors was higher among men than among women, consideration of the years of life lost shows the relationship to be reversed.

Mastitis in Hospitals.—Ranft-Häusler and Pöhn (*Deutsche med. Wchnschr.* 84:817, 1959) found mastitis in 2 of 42 mothers examined during the puerperium in a maternity hospital. Nasopharyngeal or nipple swabs taken from 40 mothers or from their infants showed pathogenic Staphylococcus aureus in 38. In 12 of these the organisms were of type M and in 20 they were of type N, and these did not give rise to any symptoms. Both were designated as hospital staphylococci. Such types were found in 8 of 25 nurses. The hospital strains which were found did not appear in the mothers or their babies until a few days after admission; in contrast, other strains could usually be demonstrated on admission. In most cases the hospital staphylococci were acquired first by the infants and then passed on to the mothers. Infection of the babies was either by direct contact with the hospital staff or by the airborne route. The authors believe these infections are dust-borne. Puerperal breast infection with virulent staphylococci is not due to the common strains which are found everywhere but to rarer and highly virulent strains.

Poliomyelitis Among Hospital Staff.—Sachtleben and Schellenberger of Munich (*Deutsche med. Wchnschr.* 84:1142, 1959) studied the frequency of poliomyelitis infection among hospital staff members because of the danger to them and to the patients in their care. Hospital staff members are particularly exposed to infection with poliomyelitis. Infection is generally by direct contact, but in most of these persons it remains subclinical. The authors carried out complement-fixation tests (CFT) for poliomyelitis on 65 physicians, technicians, and nurses. Insofar as possible all of them were tested three times a year. At the same time, serum was collected from two control groups (44 children and 71 adults). A positive CFT result was obtained in 47% of the children, 18% of the adults, and 37% of the hospital staff. Analysis of the staff by jobs revealed an excess of positive test results in the student nurses which could not be ascribed to chance. Comparison of the three different findings for each subject showed a high percentage (50%) of strong and lasting positive results among the 19-year-olds, whereas the older members of the hospital staff mostly showed weak, short-lived positive reactions. As a further control for these results the percentage of 19-year-olds in the total population giving a positive CFT result was estimated to be 24%. It is believed that all those members of the staff who gave a positive reaction had recently been infected with poliovirus. For the hospital staff in general an increased exposure to infection can be assumed.

Squill Glycosides.—W. Straube (*Ther. Gegenwart,* vol. 98, 1959) stated that the glycosides of squill have the same basic properties as the other cardiac glycosides and in their mode of action occupy an intermediate position between digitalis and strophanthin. Chemically they are steroids. A glycoside fraction of Scillaren consists principally of Scillaren A, which is slightly soluble in water but easily hydrolyzed, and Scillaren B (to the extent of one-third) which has the converse properties. Scillaren A is much more active, weight for weight, than the glycosides of digitalis. Compared with strophanthin, the glycosides of squill have a less abrupt, milder, and more constant action, which makes it easier to

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The items in these letters are contributed by regular correspondents in the various foreign countries.

regulate the dosage in clinical practice. If necessary one can always change from Scillaren to strophanthin or digitalis or vice versa.

The glycosides of squill differ from all others in having a marked diuretic and azoturic effect, which is independent of the effect on the circulation. At the same time it stimulates specific functions of the renal parenchyma, especially when there is some degenerative kidney lesion. This effect on the kidney parenchyma is supplemented by vasodilatation in the kidneys and the consequent increase in renal blood flow and the effective filtration pressure. Scillaren is particularly indicated in the various types of congenital and acquired cardiac anomalies (aortic incompetence or stenosis and pulmonary stenosis), cor pulmonale, angina pectoris, decompensated cirrhosis of the liver, and chronic renal disease with a raised nonprotein nitrogen level. In addition to its rapid action when given intravenously it is particularly valuable in hospital and general practice because it is rapidly absorbed from the intestines and is well tolerated by the alimentary tract. If digitalis or strophanthin are not well tolerated Scillaren should always be tried.

Mammary Carcinoma.—R. Kirsch of Berlin (*Zentralbl. Chir.*, vol. 84, 1959) stated that 14% of all patients subjected to radical mastectomy in 1953 in East Germany received preoperative irradiation. The author recommended this procedure. In two series of animal experiments it was shown that the incidence of metastases was raised from 3% to 80% by operation, but in a third series, in which the animals were first irradiated and then operated on, the incidence of metastases was almost completely eliminated. No local recurrences were observed in a series of 347 cancers of the breast in the years 1951 to 1953. Of these, 71 were stage 1, 186 were stage 2, 61 were stage 3, and 29 were stage 4. Of the 238 patients operated on after previous irradiation, 191 or 80.3% still had no metastases, whereas only 51 or 58.6% of those operated on without previous irradiation were still without metastases six years after operation.

The local effect of x-rays cannot be the decisive factor, since with a course of irradiation consisting of 3,000 r per field the vitality of the tumors is inhibited enough to prevent invasiveness in only 20% of patients. The defense mechanisms revoked by irradiation are effective for only a limited period and are exhausted within six weeks of the end of a course of irradiation. After this the occurrence of metastases seems to be even easier. The frequency of the incidence of metastases rises greatly if the preoperative irradiation is temporarily interrupted for any reason. The age of the patients treated had no bearing on the outcome. The author believed that preoperative irradiation works by triggering defense mechanisms which prevent the tumor particles from taking root and that the mechanisms come into play within a few hours of the first dose of radiation. Not more than six weeks should be allowed to elapse between the completion of preoperative irradiation and the operation. It seems probable that these views are valid not only for cancer of the breast but also for other types of cancer.

Gestation in Relatively Elderly Women.—Fetzer and Klees, of Giessen (*Medizinische,* 1959) stated that in recent years the number of births to primigravidas over 35 years of age has increased. Most of these were healthy women who were expecting a first child late in life for nonmedical reasons. The authors compared the course of pregnancy in 117 such primigravidas and 232 multiparas in the same age group. Cases of early or delayed menarche, menstrual disorders, and dysmenorrhea were equally common in both groups, which indicated that the first pregnancy was by no means the result of negative selection of genitally labile women.

The most difficult problem in both groups was toxicosis, especially the nephropathies. Symptoms of mild nephropathy were observed with equal frequency in both groups, but severe nephropathies were twice as common among primigravidas as among multiparas, so that the risks from this source were much greater in the first group. Correspondingly, intrauterine deaths as a result of toxemia occurred four times among the primigravidas and only once among the multiparas. The relatively unfavorable prognosis for the children of mothers with toxemia did not, however, imply an unfavorable prognosis for the mother. In no case did the toxemia prove resistant to treatment, but it is still too early to draw any conclusions about the later condition of the mothers. Postmaturity was equally frequent in both groups, but in the first group active intervention, at an earlier stage, was indicated. A comparison of the duration of labor with the duration of the second stage showed that in about 82% of the primigravidas the duration of labor was normal while the second stage was prolonged in about 16%. Uterine inertia occurred in about 11% of the primigravidas and about 4% of the multiparas. In such cases the timely and judicious administration of a spasmolytic agent is essential, whereas ecbolics should be given with caution. Surgical intervention in the case of primigravidas can also be restricted with careful observation and the judicious use of drugs without increasing the risk of infant mortality or morbidity. Probably the obstetrician should interpret the indications for cesarean section more liberally in the case of "elderly" primigravidas.

The difficult and dangerous complication of placenta praevia occurred only once among elderly primigravidas but in 3.4% of the elderly multiparas. On the other hand, manual removal of the placenta had to be performed in 8.7% of the elderly primigravidas. In these patients the second stage of labor was often prolonged. Blood loss was above normal for both groups. The "unavoidable" perinatal infant mortality was 12.8% in the first and 9.6% in the second group, almost half the infant mortality being among premature infants. The increase in the infant mortality was, however, by no means so great that patients should be advised against a late pregnancy for that reason.

Drug-Treatment of Emphysema.—H. Julich (*Ztschr. ges. inn. Med.*, vol. 14, 1959) said that the treatment of pulmonary emphysema is directed against the pulmonary insufficiency which cannot be cured but only improved, since it is based on irreversible organic changes. Theophylline preparations have long proved of use. Intravenous injection produces an increase in the minute volume of respiration and thereby a fall of several millimeters of mercury in the alveolar and arterial carbon dioxide tension. This results in an increase in the sensitivity of the respiratory center. Numerous authors have also attributed a spasmolytic, bronchodilator effect to theophylline. This is particularly important in patients with pulmonary emphysema, since most of such patients have a chronic emphysematous bronchitis with an element of bronchial spasm. The respiratory resistance is lowered by theophylline, whether it is given intravenously or intramuscularly or as an aerosol.

In order to demonstrate the spasmolytic effect, the maximum expiratory effort after a full inspiration of each of a number of patients was measured after the administration of a spasmolytic drug. The drug was always given intravenously because the absorption of aerosols varies between patients. In these experiments 12 patients, all of whom had advanced chronic pulmonary emphysema, and 8 healthy controls were given 0.226 Gm. of oxyethyltheophylline and/or 0.2 Gm. of phenyldimethylpyrazolon. The controls exhibited a slight increase in the maximum expiratory volume, whereas the emphysematous patients all showed a marked response to treatment. Of the 12 patients, 9 showed an increased expiratory volume after administration of oxyethyltheophylline, 10 after administration of phenydimethylpyrazolon, and 11 after a combination of the two. It was interesting to note the difference in response between men and women. An increase in the maximum expiratory volume was never obtained in healthy men after the combined injection, whereas the women did show an increase, an observation that had already been made in case of treatment with isoproterenol. The combination of these two preparations represents a valuable addition to the treatment of pulmonary emphysema, especially as they are both well tolerated.

Enzymatic Zonulysis for Cataracts.—W. Rohrschneider (*Klin. Monatsbl. Augenh.* 135:226, 1959) reported a series of 320 cataract operations preceded by enzymatic zonulysis. The disadvantages of this procedure included a tendency of the lens capsule to rupture, a disintegration of the anterior limiting membrane of the vitreous, and a delayed healing of the wound. On the other hand the use of alpha-chymotrypsin facilitated intracapsular extraction and therefore reduced surgical trauma, particularly in the operation for senile cataract. When enzymatic zonulysis is used on juvenile patients, the indication has to be limited to those above 10 years of age because of the possibility of vitreous adherence to the posterior surface of the lens.

Radioactive Isotopes for Plasmacytoma.—F. Weber of Mainz (*Beitr. klin. Chir.*, vol. 198, 1959) used radioactive gold intratumorally to treat two patients with plasmacytoma. Both patients treated in this way died soon afterwards with similar symptoms of intoxication. The author assumed that the body's ability to compensate was exhausted by this treatment. In view of the connection between plasmacytoma and the hemopoietic system further depression of the marrow by the application of radioactive isotopes is contraindicated.

INDIA

Segregation of Lepers.—According to the World Health Organization's second expert committee on leprosy, this disease affects at least 12 million persons throughout the world. Of these, not more than 100,000 can be given inpatient treatment at hospitals. Some 1,500,000 sufferers receive treatment while remaining with their families. The age-old custom of keeping lepers apart from the rest of the community is unnecessary from a medical point of view. The committee recommended that the legislation still existing in some countries which requires the segregation of lepers be abolished. Early treatment will prevent the unsightly deformities caused by the disease. These deformities are the basis for the popular fear of the disease. The experts concluded that though a definite susceptibility to the disease exists, resistance to leprosy can be acquired, and persons with this resistance, if they contract the disease, get it only in a mild form.

Tropical Eosinophilia.—Malik and Bhattacharya (*J. Indian M. A.*, vol. 33, Oct. 1, 1959) stated that allergy is believed to play a part in the pathogenesis of tropical eosinophilia. They studied a series of 20 patients who had this condition. The blood and plasma histamine levels were determined on samples of blood collected during the active stage of the disease and repeated in some patients after relief of symptoms by treatment with arsenic or diethylcarbamazine. Antihistamine therapy was given to some patients without benefit. The blood histamine level of most of the patients was found to be above normal during the active stage of the disease. The plasma histamine level, however, did not show a significant variation from normal, indicating that the excess histamine was located in the cellular compartment of blood of these patients. A positive correlation was observed between the blood histamine level and the absolute eosinophil count during the active stage of the illness, while no such correlation was present between the erythrocyte count and blood histamine level. After symptoms were relieved by treatment, no correlation was seen between blood histamine level and absolute eosinophil count. Although the eosinophil count decreased in all patients after treatment, the count was still high in most of them. The blood histamine level was reduced in most of them but remained high in some in spite of symptomatic relief.

NORWAY

Carriers of Hepatitis Virus.—Heistö and Julsrud (*Acta med. scandinav.* 164:349-355, 1959) reported on two blood donors who were carriers of hepatitis virus B and probably transmitted the disease to 10 recipients. It was impossible to state with certainty that each of the 10 cases of hepatitis had been caused by one of the two donors, but it was highly unlikely that more than one or two cases were of another origin. If all the observed cases of hepatitis were due to the transfusions from these donors, both had been carriers of the virus for almost four years. The authors recommended that when a patient develops hepatitis after blood transfusion, the donor or donors should be subjected to a selected group of liver function tests and all of the previous recipients of their blood should be carefully investigated. The finding of abnormal results of liver function tests or another case of hepatitis should exclude that particular donor from subsequent donations. If there is only one donor and no other source of infection is known, it is probably wise to exclude this donor from further donations even if no other case of hepatitis is detected among recipients of his blood and even if his liver function test results are normal. An attempt should be made to follow up carefully the patients who receive blood from these donors in order to detect a possible virus carrier early and thus prevent further cases of hepatitis.

SWEDEN

Circulatory Adaptation and Heart Block.—A. Holmgren and co-workers (*Acta med. scandinav.* 164:119-130, 1959) reported on three men aged 23 to 30 years and a woman aged 20 years who had complete heart block, probably congenital, the condition having been diagnosed in childhood. When in a standing position, all had large heart volumes. During work there was an increase in both auricular and ventricular rates. The physical working capacity, if estimated with the aid of the auricular frequency, was low in relation to the predicted total amount of hemoglobin in three and normal in one. Cardiac catheterization in three showed normal pressures in the right heart and the pulmonary and systemic circulation. The filling pressures for both left and right ventricle were normal. No shunt could be demonstrated.

The stroke volume was large in relation to the blood volume in both patients in whom this could be determined. Three patients had a systolic ejection murmur over the pulmonic area which was explained by the large stroke volume. The sign causing the diagnosis of heart disease was in most cases the systolic murmur, while the heart block was not noticed until later when the patients had been hospitalized either for an intercurrent disease or for further investigation of the murmur. As heart disease was diagnosed in childhood in all these patients, this would imply that the heart block either was not present or was not observed at the time of the first investigation.

Tuberculous Empyema and Antistaphylolysin and Antistreptolysin Titers.—Alf Westergren (*Acta med. scandinav.* 164:185-201, 1959) reported on a series of 181 patients who had tuberculous empyema. Staphylococcus aureus appeared in the empyema fluid of 50 patients, and other organisms also were present in some of these. In 20 there was mixed infection without Staph. aureus, and in the remaining 111 no mixed infection was demonstrated. The antistaphylolysin titer showed a rise after the onset of empyema in 96% of those patients in whom staphylococci had been found and in 38% of the others. In typical cases this elevation commenced after about two weeks and reached its maximum (8.0 units or more) after a further two or three weeks. The latter course of the titer seemed, on the whole, to be fairly well correlated with improvement or worsening of the empyema. In view of the antistaphylolysin curve it was probable that staphylococci were also implicated in the empyema in about 50% of those patients in whom antistaphylolysin elevations but not positive findings of staphylococci were recorded. In a few patients a corresponding relation between the antistreptolysin titer and the finding of beta-hemolytic streptococci could be demonstrated, but only 25 of the 181 patients exhibited rises in antistreptolysin titer in connection with the empyema, and with few exceptions the antistreptolysin curve presented a much weaker correlation with the course of empyema than did the antistaphylolysin titer.

The general behavior of the antistreptolysin titer in this series, however, illustrated the interplay of nonspecific infections, frequently without noteworthy symptoms. The two titers showed parallel rises and falls in a few patients, although on the whole they ran independent courses. Tuberculous patients often showed a tendency to high titers, but the titer elevation should invariably be interpreted as a response of the body to Staph. aureus and beta-streptococci respectively. The staphylococcic pleural process as a rule must occur through activation and spread of latent foci chiefly in the lymph nodes. The author concluded that the higher average titers in tuberculous patients were consistent with both a more profound microbial attack and a greater effort in mobilizing the antibody resources. Constitutional differences should be considered insofar as this reactive tendency is concerned. Even nontuberculous patients with genuine rheumatoid arthritis showed a similar tendency to high titers, which for antistaphylolysin was still more pronounced.

Cor Pulmonale Following Thromboembolism.—Three patients aged 43, 43, and 30 years, with chronic cor pulmonale after thromboembolism of the pulmonary artery, were studied by L. Ehrner and co-workers (*Acta med. scandinav.* 164:279-297, 1959). The thromboembolic disease started rather suddenly in these active, apparently healthy, young men, two of whom were athletes. The duration of the symptoms varied between 2 and 14 years. The onset of dyspnea was sudden. In two of the patients asthmatic symptoms developed. There were repeated attacks of peripheral thrombosis. All three of the patients had low exercise tolerance and normal pulmonary function. The cardiac output was low in relation to oxygen uptake in two patients. The authors conclude that chronic cor pulmonale after thromboembolism of the pulmonary artery should be suspected in patients who have dyspnea with normal pulmonary function tests and no signs of primary heart disease, particularly if there is a history of peripheral thrombosis. Orthopnea was a late symptom which occurred only when heart failure supervened. The diagnosis was aided by a typical roentgenogram showing centrally dilated and peripherally thin pulmonary vessels, electrocardiographic signs of right ventricular strain, and a high pulmonary vascular resistance shown by cardiac catheterization. Angiocardiography might confirm the diagnosis.

Hyperbilirubinemia and Hypersideremia.—In an investigation of nicotinic acid-induced hyperbilirubinemia and hypersideremia in 6 patients with congenital hemolytic jaundice, 9 patients with related disorders with or without definite signs of hemolytic disease, and 17 controls, Karl Gydell (*Acta med. scandinav.* 164:305-320, 1959) observed that the amount of hemoglobin broken down as measured by the rise in serum bilirubin and serum iron was greater in the patients than in the controls and that of 6 patients who had had a splenectomy the induced hemoglobin breakdown was markedly decreased. It appeared that the effect of nicotinic acid might be explained by an accelerated destruction of erythrocytes occurring mainly in the spleen. The author concluded that whatever the primary cause it seemed likely that the amount of hemoglobin broken down after an injection of nicotinic acid was finally correlated with the potentially available capacity of the spleen to destroy red blood cells, normal or defective. It thus seems possible to use the nicotinic acid test to evaluate the erythrocyte destructive capacity of the spleen. This test might be of value in the investigation of various hemolytic states and in selection of patients for splenectomy.

UNITED KINGDOM

Leukemia and Radioactive Fall-out.—The crude death rate from leukemia in Britain increased from 1.1 to 5.3 per 100,000 population in just over 25 years, and the most rapid rate of increase has been in the last 4 years. From a survey of the death rates in different counties, Phillips (*Lancet* 2:659, 1959) concluded that a possible cause of the most recent increase is radio-strontium (Sr^{90}) fall-out. In the last four years deaths from leukemia over the whole country increased by 13%, but in some counties the rise was over 50%. This was particularly true of Cumberland, Westmoreland, Caernarvonshire, and Montgomery counties, where the rise in mortality from leukemia has been as much as 140% in the last four years, although formerly they had low death rates from this cause. These are mountainous areas with high rainfall which show high levels of Sr^{90} in the soil and vegetation. The soil near the Cardiganshire-Montgomery border at a height of 1,200 ft. contained three times as much Sr^{90} as soil in Cambridgeshire, which is flat; the figures for Borrowdale in Cumberland were even higher.

This high level of Sr^{90} deposition, which is derived from radioactive fall-out, led to high figures for Sr^{90} in vegetation, milk, and animal foods, particularly where the soil contained only a little calcium. Thus milk from a special area in Cardiganshire contained 28.4 strontium units, and that from Cumberland contained 21.1 units in the period March to December, 1958, compared with a mean of 6.97 units for the whole country. The Agricultural Research Council estimated that the diet of those living in areas of high fall-out might contain 23 or more strontium units compared with the national mean of 5.9 units. Strontium followed the path of calcium in the body and was deposited in the bones. The myeloid type of leukemia was the form associated with the atom bomb at Hiroshima and Nagasaki. Figures for the types of leukemia in the different counties were not available, except for Caernarvonshire, where in the last four years the most deaths from leukemia were due to granulocytic leukemia. Although more research is needed to incriminate Sr^{90} as a cause of the increased incidence of leukemia in Britain, the preliminary data are highly suggestive.

CORRESPONDENCE

THE GROWING DEPENDENCE ON ALLIED SCIENTISTS

To the Editor:—With reference to the editorial on medicine's growing dependence on allied scientists in THE JOURNAL, Nov. 14, page 1579, it is true that the Ph.D. scientists have contributed to some impressive advances in the medical field as teachers and investigators in the medical sciences. Much of this advance has been due to research in the basic sciences. The vacancies in the departments of anatomy, biochemistry, microbiology, pharmacology, and physiology previously staffed in greater numbers by doctors of medicine have been filled in part by doctors of philosophy in these specialties. In medical schools this is probably an admirable situation, in some respects, but it is also true that the student taught by the Ph.D. in these various disciplines is probably placed at a disadvantage to his older counterpart, since his teacher does not have the clinical orientation.

There has been a national trend for the Ph.D. and other allied scientists to infiltrate the clinical aspects of the practice of medicine as well as teaching and research. This trend is apparent in the tremendous increase of so-called medical diagnostic laboratories that send out little brochures discussing various diseases, laboratory tests, and their interpretation. Since these Ph.D.'s do not have an established code of ethics, as physicians do, pertaining to commercial advertising, their infiltration is a major attempt to attain recognition in the clinical practice of medicine. It is not much of a step from the diagnosis of a disease to its treatment. This is quite apparent, since pharmaceutical houses now package their medicaments with instructions that can be followed by lay persons. It is also apparent in the dispensing of some drugs by nonmedical persons in almost every community in the United States. Some nonmedical scientists believe that they know more about medicine than physicians do.

In all areas of the country there are so-called diagnostic medical laboratories that do interpretive diagnostic work in the medical field and are staffed and owned by unqualified personnel whose education ranges from high school to a year or two of college. It seems that even the Ph.D.'s who have a diagnostic medical practice will have to cope with diagnostic laboratories that are staffed by uninformed and uneducated pseudoscientists. This trend, although subtle, is strongly apparent and presents a great danger to the welfare of the patient, when his disorder is diagnosed and treated by lay persons who do not have basic medical training. These persons have no professional or legal responsibility to their patients. It is also apparent that the American Medical Association has done little or nothing about this situation.

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HYPERURICEMIA

To the Editor:—Regarding Dr. Stanley L. Wallace's query in THE JOURNAL, Nov. 7, page 1401, about the occurrence of true hyperuricemia in patients with myocardial infarction, there is ample evidence that this does occur in the absence of azotemia or leukemia. The real question is whether this is a casual coincidence or indicative of true gout. From studies being conducted it appears that myocardial infarction, and essential hypertension as well, may be manifestations of so-called asymptomatic hyperuricemia, and a therapeutic trial with probenecid is warranted. This will require a long-term study with a large number of case reports for final evaluation.

It has also been observed that slight elevations of serum uric acid content may occur, perhaps as a stress phenomenon, in patients with diseases unrelated to gout. It is suggested, therefore, that strict criteria be adhered to before the diagnosis of gout is made and specific therapy advised. To treat everyone with a serum uric acid level of "a little over 6 mg.%" for gout would certainly be ill-advised.

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STAPHYLOCOCCIC INFECTIONS IN A MATERNITY UNIT

To the Editor:—In the paper "Surveillance and Control of Staphylococcic Infection in a Maternity Unit" by Farrer and co-workers, appearing in THE JOURNAL, Oct. 24, page 1072, evidence was presented to show that "Rooming-in was the single most important step in the termination of the outbreak." This conclusion seems to be correct. For this reason, credit should be given for the idea of rooming-in as a control measure. All the measures taken to control the epidemic appeared to be futile, and closure of the maternity unit was being considered seriously by the staff. At this point, Prof. Thaddeus Montgomery of the Jefferson Medical College was consulted. He suggested that rooming-in be instituted. This was done immediately, with the good results noted by Dr. Farrer and his associates. As far as I know, the idea originated with Dr. Montgomery and he should be credited with it.

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This item was referred to the senior author of the original article, whose reply follows.

To the Editor:—I regret the exclusion of Dr. Montgomery's name from the acknowledgment at the conclusion of the article, but as far as the authors were informed, and that includes the co-author, Dr. Sidney Werthamer, who is on the staff of the hospital, the idea of instituting rooming-in at Paul Kimball Hospital originated among the medical staff who composed the infections committee. None of the ideas on control measures that were used at Paul Kimball was "original," I dare say. Most of them have been tried before, some with and some without success. The purpose of the article was not to report an original method for controlling newborn infant-maternal infections but rather to provide epidemiologic evidence for the failure of certain control measures and the success of rooming-in. Apologies to Dr. Sawyer for our oversight.

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INTEREST IN THE PATIENT

To the Editor:—In The Journal, Nov. 7, page 1316, the following statement was made. "To the extent that a union doctor works for the union, a government doctor works for the government, an insurance doctor works for the insurance company, or a doctor works for a closed panel, a group, or a clinic, his interest in the patient is proportionately reduced." This simply is not true in the case of many of my confreres, and it will be a black day for medicine as a profession if this becomes true for most physicians. No physician ever serves his employer's best interests who fails to do the best possible on behalf of the individual patient.

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MORTALITY STATISTICS

To the Editor:—In The Journal Sept. 5, page 33, the authors of the article, "Pathological Reports for Mortality Statistics," have attempted to determine the effect of statistics on statistics. This may be of interest to statisticians, but it can hardly yield much useful information for medical scientists. The statistical method the authors used offset errors of omission by errors of commission, and vice versa. False-positive diagnoses were used to cancel out false-negative diagnoses, and the reverse. This does produce a low net change in the final statistics, but it does not give the percentage of error in death certificates. In other words, two wrongs do not make a right.

Statistics should be used as a scientific tool with the objective of arriving at new concepts or new significant data from the raw data available. To compile statistics for the sake of statistics alone is not usually very rewarding. Pathologists' death certificates should be authorized and encouraged in order to (1) help detect and punish crime; (2) insure equity where insurance and compensation are involved; (3) insure the detection of diseases of public health concern; (4) inform survivors of communicable and hereditary diseases; (5) yield data on rare diseases and those which have been discovered or redefined in recent years; (6) disclose possible relationships between diseases; and (7) study environmental factors.

There is need for creative imagination in the use of statistical methods as applied to medical problems. Pathologists' death certificates could furnish highly accurate data for statisticians and medical scientists to study. Modern electronic computers could be more widely used in this field. The paper mentioned shows a 15.2% error in death certificates in a study of 5,217 autopsy reports for the year 1956 in an area in which standards of practice are high. This means that one out of every six death certificates was in error. The number may be higher in other areas. Should we be concerned only with the "effect of autopsy reports on statistics," as the authors ask? It would be better to be concerned with the effect of autopsy reports on people, on survivors, on equity, on justice, and on medical knowledge and practice.

The authors may have been inspired to make their study by my communication to the editors (Ziegler *J. A. M. A.* 168:1260 [Nov. 1] 1958). Their study serves a useful purpose and there is no quarrel with the figures presented. It is necessary, however, to take exception to the limited manner in which they were presented and to their narrow conclusions. The authors could have stated boldly that autopsies are unnecessary because their impact on the final statistics is negligible. It is probable that their statistics are not final and that autopsies will continue to have an impact on the entire field of medical knowledge in the future as in the past. The scientific findings of pathologists should be brought to light.

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MEDICOLEGAL ABSTRACTS

Hospital Records Used in Court.—This was an action to recover damages for personal injuries sustained as the result of being struck by the defendant's car. Judgment was for the plaintiff and the defendant appealed to the court of civil appeals of Texas.

The defendant contended that the trial court erred in sustaining the plaintiff's objections to the admissibility of the hospital records, or parts thereof, relating to the plaintiff while a patient in Memorial Hospital. The court had held that they were hearsay and opinions and conclusions of physicians and therefore inadmissible. The plaintiff conceded that all portions of the hospital records were admissible except those portions involving medical opinions or conclusions.

The court decisions are at variance as to the admissibility of hospital records consisting of diagnostic findings and opinions by attending physicians. Many courts hold that such records are regular business entries and are therefore admissible provided the declarant appears to have the necessary qualifications to render an expert opinion. Other courts oppose the admission of medical diagnoses on the ground that opposing counsel is deprived thereby of the opportunity for cross examination. Doctors frequently disagree when it comes to a diagnosis and therefore medical opinions and diagnoses do not have the inherent guarantee of accuracy of routine business entries.

The court said that factual statements made by physicians and contained in the hospital records are admissible in the same manner as factual statements made by nurses and other employees of the hospital in connection with the routine business of the hospital. For example, medical statements, made as routine entries in the course of hospital business, consisting of reports of the patient's temperature, blood pressure, pulse, medicines and treatment prescribed, external bruises, skin rash, alcoholic breath, lacerations or injuries observable to persons generally, routine laboratory tests, expressions of pain, noticeable external physical marks or defects, and similar facts not involving medical opinions, should be admitted. Where, however, the statement of the physician consists of an opinion, conclusion or diagnosis based on his medical examination or findings of conditions not obvious or patently observable to persons generally, it should be excluded. In such a case the doctor should be brought into court where he might be cross-examined by opposing counsel. The decision as to whether the record falls within the one category or the other, said the court of appeals, should be left largely to the sound discretion of the trial court. The court, therefore, concluded that the hospital records in question were not erroneously excluded. The judgment of the trial court in favor of the plaintiff was affirmed.—*Martinez v. Williams*, 312 S. W. (2d) 742 (Texas, 1958).

Privileged Communications: Physical Examination of Plaintiff.—This was a petition to obtain the pretrial inspection of a certain medical report. From an adverse decision, an appeal was taken to the district court of appeal, third district, California.

The petitioner filed a malpractice action against a physician. Subsequently, the physician's attorneys requested that the petitioner be examined by another doctor. The petitioner acquiesced in this request and voluntarily submitted to a physical examination by the second doctor, whose report was thereafter transmitted to the attorneys for the defendant. The petitioner did not receive a copy of this medical report and her request for such copy was refused by the attorneys for the defendant on the ground that the information contained therein was within the attorney-client privilege.

In the opinion of the court of appeal, the attorney-client privilege is to protect communications between client and attorney. When the plaintiff is examined by a physician for the purpose of informing his own attorney as to his physical condition, the medical report is privileged. When the plaintiff is examined by a physician for the purpose of informing the defendant's attorney as to his physical condition, however, the circumstances are entirely different and the same rule is not applicable. In the instant case, the communication was by plaintiff to a physician engaged by counsel for defendant. In such a case, the necessary element of attorney-client relationship is lacking and the essential feature of confidential intent in revealing information is also lacking. Furthermore, the court of appeal stated, the submission of plaintiff to examination by a doctor employed by defense counsel is adversary rather than confidential. Since the report in question was made possible only through the cooperation of the plaintiff who voluntarily submitted to the examination, there is no reason to deny him a copy of it. The court, therefore, concluded that the medical report requested by the petitioner was not a privileged communication and that the lower court erred in denying the petitioner's motion for an inspection of it. *Jorgensen v. Superior Court for the County of Sonoma*, 329 P. (2d) 550 (Calif., 1958).

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Bland and Infected Arteriosclerotic Abdominal Aortic Aneurysms: A Clinicopathologic Study. R. L. Sommerville, E. V. Allen and J. E. Edwards. Medicine 38:207-221 (Sept.) 1959 [Baltimore].

The authors collected 178 consecutive cases of arteriosclerotic aneurysms of the aorta, measuring 2 cm. or more in diameter, from 20,201 autopsies performed at the Mayo Clinic between 1925 and 1954. Examination of specimens of the aorta with aneurysm showed that 172 were bland (noninfected) aneurysms and 6 were infected aneurysms. A review of the clinical records of the patients showed that 125 were men and 53 were women. Of the 172 patients with bland aneurysms, 32 had symptoms that could be attributed directly to the aneurysm (diagnostic symptoms), 42 had symptoms that may have been due to the aneurysm or to an associated disease process or both (equivocal symptoms), and 98 were entirely asymptomatic. Abdominal pain was present in 27 of the 32 patients with diagnostic symptoms, and rupture of the aneurysm had occurred in 24 of these 27 patients. Pain in the back occurred in 24 of the 32 patients with diagnostic symptoms. Only one aneurysm in the 27 patients with abdominal pain measured less than 5 cm. in diameter.

Information regarding the duration of life from the onset of diagnostic symptoms or objective evidence of the aneurysm was available in 38 of the 172 patients; 25 of the 38 lived less than one year and 22 died within the first month, 19 of them as a result of rupture of the aneurysm. A pulsating abdominal mass, noted in 23 of the 172 patients, was the commonest physical finding. Seventeen of these patients, all of whom had aneurysms measuring more than 4.5 cm. in diameter, had both diagnostic symptoms and a pulsating abdominal mass. A palpable abdominal mass was absent in 111 patients; yet 23 of them had aneurysms of "diagnostic" size (more than 4.5 cm. in diameter). Thus, slightly more than 50% of the aneurysms of detectable size were not recognized clinically.

Roentgenographic studies were performed on 41 patients, with findings diagnostic of aneurysm noted in 13. Of the 172 bland aneurysms, 76 were fusiform, 93 were saccular, and 3 were cylindrical. A total of 55 aneurysms measured 4.5 cm. or more in diameter, and 30 of these large aneurysms were associated with diagnostic symptoms or signs. Only one of the 117 small aneurysms (less than 4.5 cm. in diameter) produced symptoms that could be related directly to the aneurysm. Rupture of the aneurysm occurred in 31 (18%) of the 172 patients; only one of these aneurysms measured less than 4.5 cm. in diameter. Death was attributed to rupture of the aneurysm in 30 patients. Coronary insufficiency accounted for 19 deaths; a recent myocardial infarct was found in 10 additional patients. Otherwise, the causes of death were variable. Hypertension was present in 91 (60%) of the 152 patients for whom such information was available. The distribution in the 2 sexes was about equal. All the patients had moderate to severe coronary and aortic sclerosis.

The arteriosclerotic abdominal aortic aneurysms of the 6 patients with infected aneurysms were characterized by a prominent degree of inflammation. These infected aneurysms presented no distinctive clinical features. Pathologically, they were characterized by an acute inflammatory reaction involving the intima and media, with necrosis and destruction at the aortic wall. Rupture occurred in 4 cases. Bacterial colonization was noted in 4 of the 6 cases.

From the data presented, it appears that an arteriosclerotic aneurysm of the abdominal aorta assumes dangerous potentialities once it reaches 4.5 cm. in diameter. Yet it is only when aneurysms are at least this size that they can be detected with any degree of accuracy by physical examination.

Thrombotic Thrombocytopenic Purpura. S. Persson. Nord. med. 62:1270-1272 (Aug. 20) 1959 (In Swedish) [Stockholm].

Thrombotic thrombocytopenic purpura is characterized by the triad of hemolytic anemia, thrombocytopenic purpura, and neurological symptoms of varying degree. As a final element in the diagnosis, the presence of hyaline thrombi in arterioles and capillaries must be demonstrated by biopsy or at autopsy. The sites of predilection are the heart,

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The place of publication of the periodical appears in brackets preceding each abstract.

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adrenals, kidneys, spleen, and liver. There is always a slight enlargement of lymph nodes, and splenomegaly and hepatomegaly are usual. In general, the disorder manifests itself as a frequently febrile, grave, general disease. Clinically it somewhat resembles lupus erythematosus disseminatus, polyarteritis nodosa, and hereditary hemolytic anemia. The duration is from a few days to several years, but the course is usually rapid, with fatal outcome. The etiology is uncertain. No satisfactory therapy is known. In most cases diagnosis is made at autopsy. In the case reported, in a woman, aged 43 years, there had been hemolytic anemia for 6 months before the development of thrombocytopenic purpura and neurological symptoms, with rapidly progressive renal insufficiency. At autopsy hyaline thrombi were found in the small blood vessels.

The diagnosis of thrombotic thrombocytopenic purpura depends on the histopathological establishment of hyaline thrombi in the smaller blood vessels simultaneously with the clinical establishment of hemorrhagic thrombocytopenia. The demonstration in the case reported of thrombocyte agglutinins is of special interest. Two remissions were attained with prednisone, the first lasting over 4 months. Treatment with cortisone and cortisone derivatives has previously been regarded as ineffectual, but further tests with cortisone steroid treatment are advised. Especially in patients with demonstrable erythrocyte and thrombocyte agglutinins, a favorable effect may be expected.

The Diagnosis and Treatment of Addison's Disease. B. Hudson. Australasian Ann. Med. 8:182-194 (Aug.) 1959 [Sydney, Australia].

The author designates the use of corticotropin (ACTH) in diagnosis, the development of simple methods for chemical assay of adrenocortical hormones in urine and plasma, and the availability of potent adrenal steroids for treatment, as the reasons for the significant progress in the management of Addison's disease (adrenocortical hypofunction). He analyzes the clinical manifestations and course of Addison's disease and the usefulness of the newer procedures on the basis of experiences in 21 patients observed over the past 6 years. There were 16 females and 5 males. Twenty patients are alive and able to lead active and normal lives. One patient died in Addisonian crisis at the time of diagnosis. These patients have been drawn from a larger series of 41 cases in which the diagnosis of adrenal insufficiency was suspected. The conditions with which Addison's disease is commonly confused include states of malabsorption, occult malignant disease, chronic renal disease, anorexia nervosa, other anxiety states, and orthostatic hypotension.

Laboratory procedures included estimation of urinary steroid excretion, adrenocortical response to ACTH, changes in circulating eosinophils, electrolyte and other plasma values, water excretion, glucose tolerance, and hematological data; also investigation of tuberculous infection, of the melanocyte stimulating hormone content of the blood, of the autoimmune complement-fixing (AICF) antibodies, and the use of 9-alpha-fluorohydrocortisone. In evaluating these different diagnostic investigations, the author emphasizes the need of ACTH stimulation, pointing out that after ACTH stimulation the rise in excretion of both 17-hydroxysteroids and 17-ketosteroids was minimal in 11 and 12 of the 14 cases respectively. Case histories are cited to illustrate the value of ACTH stimulation.

It has been generally accepted that adrenal tuberculosis was the commonest cause of Addison's disease. Recent reports, however, indicate that tuberculosis is now responsible for the disease in less than 50% of cases. When it is not due to tuberculosis, Addison's disease has been ascribed to "adrenal atrophy." The concept that spontaneous adrenal atrophy may have an autoimmune basis was suggested by Anderson and associates in 1957; these investigators demonstrated the presence of AICF antibodies to human adrenal tissue in the serum of 2 of 8 patients with nontuberculous Addison's disease. The serum of 2 of 9 patients in the present series showed AICF antibodies when tested against human adrenal tissue, but the titer in both instances was weak and of doubtful significance. However, further investigation would seem warranted. When the disease is due to tuberculosis, the history has been relatively short—from weeks to a few months—in contrast to nontuberculous Addison's disease, in which the illness can often be traced over a number of years.

The treatment of the 21 patients is outlined. The condition of all of them have been successfully maintained with cortisone or hydrocortisone for periods of up to 6 years. Eight patients receive mineralocorticoid supplement. The outlook for the patient with Addison's disease has improved with the introduction of newer methods for diagnosis, particularly ACTH stimulation, and with the availability of cortisone or hydrocortisone for treatment.

Pseudoxanthoma Elasticum: A Systemic Disorder. M. G. Robertson and J. S. Schroder. Am. J. Med. 27:433-442 (Sept.) 1959 [New York].

Pseudoxanthoma elasticum may be associated with ophthalmological, gastrointestinal, and peripheral vascular lesions. The occurrence of angioid streaks of the retina in association with pseudoxanthoma elasticum constitutes the Grönblad-Strandberg syndrome, in which progressive retinal changes may lead to serious impairment of vision and even to blindness. Gastrointestinal hemorrhage may result from vascular changes in the mesentery with secondary mucosal involvement at any level of the gastrointestinal tract. Peripheral vascular lesions in the extremities may lead to weak pulses, abnormal oscillometric findings, and intravascular calcifications. Although the eye and skin findings have for years attracted the attention of ophthalmologists and dermatologists, the systemic nature of pseudoxanthoma elasticum has not received sufficient attention among internists, so that in some patients the disorder may not have been recognized.

The authors present the histories of 3 patients. The first, a 47-year-old woman, had experienced unexplained gastrointestinal bleeding at recurrent intervals for 5 years. Examination revealed the skin changes of pseudoxanthoma elasticum, and examination of her retina revealed angioid streaks. It is possible that the gastrointestinal bleeding episodes represent intestinal mucosal changes secondary to involvement of the mesenteric vessels with this disease. The second patient, a 61-year-old woman, gave a 6-month history of migratory polyarthritis with swelling, heat, pain, tenderness, and fever. A biopsy specimen of the skin revealed the changes of pseudoxanthoma elasticum. Ophthalmologists confirmed the existence of angioid streaks. Roentgenograms showed vascular calcifications in the pelvic region. The third patient, a 54-year-old woman, in addition to Marfan's syndrome (arachnodactyly), had angioid streaks of the retina. This observation, together with a history of gastrointestinal bleeding and the finding of calcification of the arteries of the arm, suggested the possibility of a "mixed" picture of Marfan's syndrome and pseudoxanthoma elasticum. The diagnoses were (1) congenital defect of elastic tissue, giving a mixed picture of Marfan's syndrome and pseudoxanthoma elasticum, (2) secondary anemia, and (3) rheumatoid arthritis. The condition of the third patient seems to suggest a bridging of the gap between the diseases of connective tissue, on the one hand, and the congenital mesodermal dystrophies, on the other, in that migratory polyarthritis was present in addition to Marfan's syndrome and pseudoxanthoma elasticum.

SURGERY

The Surgeon's Tactics in the Treatment of Acute Cholecystitis. B. K. Ossipov. Surgery 46:507-512 (Sept.) 1959 [St. Louis].

Although growing numbers of patients are being operated on during acute cholecystitis, there is no general agreement as to the indications for this treatment or as to the choice of anesthesia. According to the author, this problem was discussed by Russian surgeons at a meeting in 1956. Of 2,505 patients operated on in connection with acute cholecystitis in 25 Moscow hospitals, 275 died; thus, the mortality rate was 11%. In individual hospitals the postoperative mortality varied from 7.75 to 19.5%. Postoperative deaths in acute cholecystitis are mainly due to tardy application of the patients for medical advice as well as to their belated hospitalization for surgical treatment. Peritonitis accompanied by cardiovascular insufficiency and pneumonia is the chief cause of death.

At a surgical clinic of the Central Postgraduate Institute for Physicians in Moscow, Vishnevsky developed a method of local infiltration anesthesia, which has been used at that clinic in the surgical treatment of patients with acute cholecystitis for the last 25 years. Local procaine anesthesia, unlike ether narcosis, does not produce intoxication, nor does it exert a noxious influence on the liver. It is simple, convenient, and facilitates the operative technique. Anesthetization must precede each stage of the operation. A paranephric procaine block precedes the operation, and then the peritoneal wall is anesthetized. The skin, the subcutaneous fatty tissue, the muscles, and the extraperitoneal fatty tissue are subjected to anesthesia in succession. After incising the tissues of the abdominal wall, a solution of procaine is introduced into the extraperitoneal fatty tissue from the inside of the abdominal cavity. Then the procaine solution is introduced into the root of the mesentery of the liver angle of the large intestine (flexura hepatica) beneath the lower edge of the duodenum, from whence the fluid spreads into the splanchnic region. Finally, the procaine solution is introduced under the peritoneum covering the hepatoduodenal ligament. Now, beginning with this ligament, subject, of course, to the absence of any destructive changes in its wall, it is possible to start investigating the state of the gallbladder and of the biliary tract.

Local procaine anesthesia not only is an anesthetizing factor but also aids in normalizing the trophic function of the nervous system and in favorably influencing the inflammatory process, particularly the concomitant pancreatitis. A bilateral paranephric procaine blockade in acute cholecystitis favorably changes the course of the inflammatory process, unless the disease takes a destructive form. In the latter case the paranephric blockade facilitates the differential diagnosis.

When a patient with acute cholecystitis is admitted to the clinic (which often happens at night), the surgeon first of all performs a bilateral paranephric procaine block. Soon after the blockade (sometimes within 2 or 3 hours), the inflammatory process may show a tendency to subside. The pains disappear, the temperature returns to normal, the leukocytosis declines, and the local phenomena abate. After a thorough examination the advisability of surgical treatment is decided upon. If after several hours the inflammatory process shows no tendency to regress, operation is performed within 24 hours after admission. Patients with acute cholecystitis should be placed, not in medical, but in surgical divisions of hospitals and must be under the observation of surgeons from the very beginning. Cholangiography and manometry are usually performed during operation. Repetition of cholangiography after the operation makes is possible to recognize and to diagnose the character of the biliary obstruction and to establish the patency of the biliary ducts.

Leiomyosarcoma of Meckel's Diverticulum. R. B. Fahim and J. H. Pratt. Minnesota Med. 42:1269-1273 (Sept). 1959 [St. Paul].

The authors report on a 47-year-old man and a 61-year-old woman with leiomyosarcoma of Meckel's diverticulum, who were admitted to the Mayo Clinic. Three cases of leiomyosarcoma of Meckel's diverticulum were reported previously from the Mayo Clinic, and 7 additional cases of this condition were collected from the literature. Of the 12 patients with leiomyosarcoma of Meckel's diverticulum, 9 were men and 3 were women. Their ages ranged from 22 to 66 years. The presenting symptoms were melena, intestinal obstruction, pain, perforation, and peritonitis. Melena, which was massive in one of the authors' 2 patients, was also the presenting feature in 2 of the other 10 patients; in one patient it was severe enough to necessitate repeated blood transfusions, and in the other it was moderate and associated with secondary anemia. Intestinal obstruction was the chief complaint in 3 patients; in all of these the tumor was palpable and located in the pelvis, and obstruction was due to the extrinsic pressure of the tumor. Pain was the presenting feature in 2 patients; perforation of a necrotic tumor and peritonitis were the presenting features in 1 patient.

The 12 patients were operated on; the excised tumors varied in size from 8 to 15 cm., but were uniformly large. In those patients in whom a histological diagnosis was available, the tumors were described as low-grade tumors (Broder's classification). Neither metastasis to the liver nor direct spread to the peritoneal surfaces was present. Spread to the lymph nodes was reported by one of the other workers in one patient. The diagnosis of the tumor as one arising in a Meckel diverticulum was based on the presence of a remnant of the diverticulum in 7 patients and on the position of the tumor on the wall of the intestine and its location in 4 patients; in one patient the criteria were not available. The presence of a remnant of Meckel's diverticulum was the most conclusive evidence of the origin of the tumor. In the absence of remnants of the diverticulum, as in advanced leiomyosarcomas of Meckel's diverticulum, the enlarged remnants of the vitelline vessels proved to be of great diagnostic importance.

The vitelline vessels, which were described previously in 2 patients reported from the Mayo Clinic, were prominent in the 61-year-old woman; they consisted of a sizable artery and its companion vein that arose from the mesentery of the ileum and crossed the intestine to supply the tumor. Under normal circumstances these vessels are of smaller size than other vessels, but they can be identified easily in the mesentery of a Meckel diverticulum. With the advent of malignant change they may assume extremely large proportions to maintain a blood supply equal to the growth of the tumor. Removal of local growth and accessible metastatic lesions is extremely important. Lymphatic spread is rare, and, therefore, resection of a deep wedge of the mesentery of the small intestine is unncessary. Both of the authors' patients made an uneventful recovery, and one of them survived 5 years, only to die subsequently of a heart attack.

Treatment of Tuberculosis of the Spine. M. C. Wilkinson. Brit. M. J. 2:280-282 (Aug. 29) 1959 [London].

The author reports on 138 operations performed on 128 patients with tuberculosis of the spine during the period from 1948 to 1958. Antibiotic cover was given for 14 to 18 weeks in most instances. Provided that no bone destruction was occurring, an interval of 3 or 4 months might be allowed to elapse before operation in the case of adults; in children the interval might be shorter. Operation then became easier and safer because inflammatory hyperemia was less. There was no operative mortality. The most important operative complication, encountered twice, was tension pneumothorax, due to puncturing of the pleura. The author believes that for successful and safe operating 2 things are essential: (1) a high degree of anesthetic skill, because, if the patient gets anoxic, oozing occurs, impairing vision of the operative field, and (2) a high standard of bone radiography, because definition of the abscess and of cavities and sequestra may be difficult even with good radiography. Of 8 patients who recovered with unstable fibrous ankylosis, some had extensive vertebral destruction, but improved to the extent that they were leading normal and useful lives.

The majority of the patients treated by direct operation on the lesion had disease of the mid and lower thoracic and thoracolumbar portions of the spine. In spite of the unfavorable localization of the lesion, most of these patients got excellent results. Twenty-one patients required readmission for further treatment, and, with the exception of one who was still completing treatment, they all recovered. There were only 2 deaths in the entire series. One woman died of tuberculosis, having been reported to have developed tuberculous meningitis 3 years after her discharge. Another patient died of nonspecific pneumonia 3 years after discharge. The mortality rate of less than 2% of the 128 patients compares very favorably with the mortality rate before the introduction of antibiotics, which for most series, centering on a 5-year follow-up, was approximately 30%. The average duration of treatment of patients subjected to direct operation was 9.7 months.

The author believes that, by the direct operative treatment of tuberculosis of the spine, good and relatively speedy results can be obtained, with the early return of the patient to full employment. With a 2-rib costotransversectomy approach, the operation is safe if done with precision and deliberation, with the aid of preliminary constitutional and antibiotic therapy, and with sufficient antibiotic cover. By the costotransverse route adequate access can be gained to 2 or 3 vertebral bodies.

First Experiences with Extracorporeal Circulation in Heart Operations. E. Derra and B. Löhr. German M. Month. 4:291-294 (Sept.) 1959 (In English) [Stuttgart, Germany].

The authors describe observations on 31 patients who underwent cardiac surgery with the aid of extracorporeal circulation in the department of surgery of the Medical Academy, Düsseldorf. The Gibbon-Kirklin pump-oxygenator was used, after its use had been studied at the Mayo Clinic. The authors stress the importance of a thoroughly trained team for heart operations with extracorporeal circulation. In the hands of such a team, the Mayo-Gibbon pump-oxygenator has proved its worth, and no accident or complications attributable to technical defects have occurred. The rate of perfusion employed was 1.9 to 2.4 liters of blood per square meter of body surface per minute. Thirteen patients were operated on at normal body temperature, and 18 under hypothermia, cooling and rewarming being controlled by means of the heart-lung machine. A temperature of 30 C (86 F), measured centrally, seemed suitable, but owing to the small number of cases, a final conclusion on this point cannot be made.

Ventricular septal defects were repaired in 25 patients. This number included 7 in whom other anomalies were present in addition to the ventricular septal defects. In 6 of the patients the ventricular septal defects were multiple. Direct suture was all that was necessary in the patients with the ventricular septal defects; an implant was necessary in only 2 of them. There were 2 operative deaths among those with isolated defects of the ventricular septum, and 2 among the 7 patients who had additional anomalies. There were 2 other operative deaths (a total of 6 in the 31 patients). One of the 4 patients with the tetralogy of Fallot died. Of the 2 patients with ostium primum defects, with complete splitting of the mitral valve and a defect or fissure in the tricuspid, one died of heart block 21 days after the operation. The postoperative course was free from complications in 23 of the patients. Hemorrhage made it necessary to reopen the chest in one patient, but recovery was then uneventful. In another patient a soft-tissue infection developed 5 days after the operation, but it cleared up with conservative treatment.

Clinical and Hemodynamic Findings in Acquired Disorders of the Tricuspid Valve. P. F. Angelino, V. Levi, L. Dughers and D. Tartara. Minerva cardioangiol. 7:305-319 (July) 1959 (In Italian) [Turin, Italy].

Diagnostic and therapeutic problems were studied in a group of 27 patients who had a lesion of the tricuspid valve combined with other acquired valvular lesions. Pure mitral stenosis was present in 16 patients, pure mitral stenosis associated with aortic stenosis in 2, pure mitral stenosis associated with double aortic disorder in 2, and a mitral insufficiency related to stenosis in 7. Clinical diagnosis of the lesion of the tricuspid valve was confirmed at operation on 20 patients. Mitral commissurotomy was performed on 17 patients. Simultaneous commissurotomy on both the mitral and the tricuspid valve was performed on 3 patients. Seven patients were not operated on because of poor hemodynamic condition.

Of 13 patients who were operated on for pure mitral stenosis, late results were good in 3 patients, fair in 3, and poor in 4. Three patients died. Of 7 patients who were operated on for mitral stenosis combined with insufficiency, late results were poor in 6 patients. One patient died. Ascites, icterus, and prominent pulsation of the jugular and hepatic veins appeared in less than one-half of the patients, whereas the respiratory symptoms, such as dyspnea on exertion, paroxysmal dyspnea, orthopneic position, pulmonary edema, and spitting of blood were more frequent. Medical treatment could correct only certain types of insufficiency of functional nature or associated slight mitral disorder. Surgical therapy was efficacious in the treatment of pure stenosis of the tricuspid valve or a condition in which this disorder was the main feature. It was also effective in correcting functional insufficiency of the tricuspid valve associated with pure mitral stenosis.

Commissurotomy and Pregnancy. P. H. Benavides de Anda, A. Estendía Cano and N. Gómez Patiño. Gac. méd. Mexico 39:355-365 (May) 1959 (In Spanish) [Mexico, D. F.].

Forty women, between the ages of 22 and 35 years, with mitral stenosis, underwent commissurotomy at the Instituto Nacional de Cardiología in Mexico City. There were both multiparas and primiparas. The mitral area was less than 1 sq. cm. in all the patients except 2 in whom it was, respectively, 2 and 2.5 sq. cm. Twelve patients were pregnant. Commissurotomy was ample in 9 of these patients and partial in 3. Pulmonary capillary hypertension, which was severe before the operation, greatly diminished, or entirely disappeared, afterward. In each case the pregnancy followed a normal course to full term, and the delivery was normal; all the infants were born normal and alive. Twenty-eight patients were not pregnant. Commissurotomy was ample in all these patients, except in 6 in whom it was partial. Twenty-three patients had had severe pulmonary capillary hypertension during previous pregnancies and before commissurotomy. After the operation pulmonary capillary hypertension greatly diminished, or disappeared, in all the patients except one in whom the mitral area covered 2 sq. cm. Five patients had not had mitral symptoms during previous pregnancies; they complained of repeated abortions between the 2nd and 5th months of pregnancy. The 28 patients who were not pregnant at the time of commissurotomy became pregnant after the operation. Their pregnancies followed a normal course to full term, with normal delivery and with the infants born alive and normal.

The authors conclude that commissurotomy favorably modifies the course of pregnancy by controlling the mitral obstacle to the circulation, with consequent normalization of pulmonary capillary hypertension. The improvement obtained from commissurotomy during, before, or after pregnancy persists in further pregnancies. Pulmonary capillary hypertension in pregnant women with mitral stenosis is a definite indication for commissurotomy.

Indications For Surgery in Funnel Chest. V. Paltia, K. V. Parkkulainen and M. Sulamaa. Ann. paediat. Fenniae 5:183-194 (no. 3) 1959 [Helsinki].

The authors report on 81 children with funnel chest, who were treated surgically at the Children's Hospital of the University of Helsinki between 1951 and 1957. There were 26 girls and 55 boys. their ages ranging from birth to 7 years. The funnel deformity was observed immediately at or soon after birth in four-fifths of the cases, and progression was observed in more than half of the cases. Fifty-seven patients had one or several symptoms, such as tiredness, pain, dyspnea, and recurrent respiratory infections. Respiratory infection was commoner in patients with a deep funnel than in those with a shallow depression. In 24 patients no subjective symptoms were reported. The commonest electrocardiographic findings were rotation of the heart on its axis and cardiac displacement. Only in 20 of the 81 children were no cardiac changes, radiographically or electrocardiographically, demonstrable. Changes in the heart were decidedly commoner in those children whose deformity had been considered deep than in the children with a shallow depression. Operative indications, besides changes in the heart and respiratory symptoms, were progressing deformity and cosmetic and psychological factors. Seventy of the 81 patients have been operated on according to the authors' own method, (J. A. M. A. 170:733 [June 6] 1959), with very satisfactory results; there were no fatalities and no severe complications.

This study clearly demonstrates that funnel chests tend to progress with age and that the larger the deformity, the more difficult is the operation. Therefore, it is suggested that surgical treatment should be carried out at an early age, whenever there is either a large deformity or a progressive tendency, or any other clear indication. Because of the technical difficulties and the increased rate of complications, treatment with regard to indications in patients over 6 years of age should be *slightly* more conservative, but postponement of surgical intervention in cases with clear indications is of no benefit.

Extrahepatic Portal Bed Block in Children: Pathogenesis and Treatment. H. W. Clatworthy Jr. and E. T. Boles Jr. Ann. Surg. 150:371-383 (Sept.) 1959 [Philadelphia].

Portal hypertension due to extrahepatic block in the portal venous system is generally the result of acquired thrombosis and leads to a definite sequence of events. Children with this condition often have an extremely high portal pressure and poorly developed collateral circulation, and present themselves with ascites, growth failure, and chronic anemia secondary to blood loss. After a variable period of time and with appropriate therapy, recanalization of the thrombotic process and the gradual development of collateral venous channels lead to disappearance of the ascites, and for a period these children may grow and develop in a near normal fashion. Later, usually after several years, they become clinical problems, with either massive upper gastrointestinal hemorrhage from esophageal varices or secondary hypersplenism. Eleven infants and children were observed at the Columbus (Ohio) Children's Hospital in various phases of this process in the past 8 years.

Observations on these 11 children convinced the authors that no definitive surgical procedure is indicated in the infant with ascites. Management consists of the periodic administration of blood or albumin and paracentesis as necessary to control symptoms. After a variable period of months, the ascites will disappear, and a normal growth pattern will return. The child under 4 years of age with bleeding from esophageal varices should be treated without operation if at all possible. Even repeated episodes of bleeding are usually well tolerated, since liver function is normal. If direct control of such bleeding becomes imperative, transesophageal ligation of the varices is probably the best procedure to bargain for time and growth. If this is not adequate, a proximal gastrectomy with detachment of the lower half of the esophagus or esophagogastrectomy with jejunal or colonic interposition may be done.

Over the age of 4 years, control of bleeding is best accomplished by a splenorenal shunt if the splenic vein is of good size. A centrally placed anastomosis in which a short proximal segment of splenic vein is used has theoretical advantages over the conventional technique. For the patient with no available splenic vein, usually because of a previous splenectomy, an effective shunt may be possible with a side-to-end superior mesenteric vein to inferior vena cava anastomosis. Success of this shunt depends primarily on the presence of a normal superior mesenteric vein or retropancreatic venous lake free of active thrombotic disease.

Studies of Local Gastric Cooling as Related to Peptic Ulcer. O. H. Wangensteen, P. A. Salmon, W. O. Griffen Jr. and others. Ann. Surg. **150**:346-360 (Sept.) 1959 [Philadelphia].

Although experience at the University of Minnesota Medical Center in Minneapolis confirmed that local gastric cooling has definite merit in the control of massive gastric hemorrhage, the following problems still require answers: Will local gastric cooling alone suffice? Should the patient be taken to the operating room with the cooling device in situ as soon as the vital signs are stabilized? Should there be a delayed operation?

Local gastric hypothermia is accomplished by circulating a cold solution of equal parts of alcohol and water through an indwelling gastric balloon. By regulating the temperature of the inflowing fluid at 0 to —5 C (32 to 23 F), the gastric mucosa of man and dog can be maintained at a temperature in the range of 10 to 14 C (50 to 57.2 F). At this temperature, peptic activity is essentially suspended; gastric secretion is diminished 75% or more; and the gastric venous outflow, which reflects arterial inflow, is decreased approximately 66%. Surface warming of the patient with an electric blanket suffices to maintain a normal body temperature. Preliminary studies suggest that direct perfusion of the gastric mucosa may prove feasible. It is a more efficient method of cooling, in that every cranny of the stomach is in contact with the cooling solution, but it demands special attention to avoid esophageal reflux.

To date 30 patients with bleeding from the upper gastrointestinal tract have been subjected to local gastric cooling. A few of these have had more than one episode of hemorrhage. Fourteen patients bled from a duodenal ulcer; in 11 of these there was a history of previous ulcer symptoms. Three additional patients bled acutely after either severe trauma or massive steroid therapy. Cessation of hemorrhage occurred in all. However, massive bleeding recurred in those under stress or steroid therapy. Cooling was effective again in 2 of these patients. Local gastric cooling, employing the balloon, was used in 2 patients with gastric ulcer. The hemorrhage was controlled in both of them.

Five patients with portal hypertension and with massive bleeding from esophageal varices were subjected to local gastric esophageal cooling. One of these, a patient with cirrhosis, was admitted in deep coma; his bleeding was rapidly controlled, but persistent coma and progressive liver failure resulted in death. A second patient was inadequately controlled, and transesophageal ligature of the bleeding varices was carried out; he died in the early postoperative period. A definitive operation was performed after gastroesophageal cooling on 3 patients. In one with hepatic cirrhosis, a portacaval shunt was established; in the other 2, both of whom had extrahepatic obstruction, jejunal replacement of the esophagus with Roux-Y reconstruction was carried out. All 3 patients are doing well.

Gastric cooling was resorted to also in such conditions as hemorrhagic gastritis, postoperative bleeding, and disseminated malignancy. Complicating factors, including sepsis, steroid therapy, and deficiencies in the blood-clotting mechanism, made many of these cases debatably suitable for achieving arrest of hemorrhage by local gastric cooling. Nevertheless, control of hemorrhage was achieved in a number of them. The volume and proteolytic activity of gastric juice appear to rebound after cooling, a circumstance which suggests the need for early operation if the intragastric or intraduodenal infusion of a continuous, cold skim-milk drip, administered through an indwelling nasogastric tube, fails to control the situation. The use of skim milk has proved successful in the postcooling management of the duodenal and gastric ulcer patients. It is not unlikely that direct perfusion of the gastric lumen with a cold solution may prove to be an adjuvant measure in accelerating the healing of ulcers.

NEUROLOGY & PSYCHIATRY

Neurosurgical Aspects of Some Complications of Tuberculous Meningoencephalitis. F. R. Oliveros and J. P. Guitián. Rev. españ. oto-neuro-oftal. **18**:170-181 (May-June) 1959 (In Spanish) [Valencia, Spain].

The frequency of neurological complications of tuberculous meningitis has stimulated the development of new therapeutic procedures in neurosurgery. The authors analyze the results of their neurosurgical techniques (liberation of exudates, continuous ventricle drainage, and radical extirpation of a tuberculoma) as applied to 7 patients with neurological complications of tuberculous meningitis, who were treated at the University pediatrics clinic in Santiago de Compostella, Spain. The youngest patient was 7 months old; the oldest was 16 years. Adjuvant therapy consisted in the administration of prednisone to 4 patients and of hydrocortisone to 3. The results were excellent in 2 patients, good in 2, and ineffective in one who survived but in whom an irreversible spinal block remained; 2 patients died.

Ventricle drainage was performed in 3 patients, 2 of whom had hydrocephaly with increased intraventricular pressure causing intense cerebral disturbance. In one patient the continuous growth of the cranial perimeter was arrested, and considerable clinical improvement was obtained. The second patient, who had a 17-cm. intracranial pressure, died. The third patient, who was suffering from hemiplegia and ocular paralysis, obtained great relief of his symptoms. Liberation of optochiasmatic exudates was performed in one patient with papillary amaurosis; there was satisfactory improvement of all symptoms, including the amaurosis. It should be pointed out that in any case of amaurosis with papillary atrophy, or anoxia of the optic axis, the operation must be performed before the photomotor reflex disappears in order to restore vision. Extirpation of a tuberculoma from the right cerebellar hemisphere was performed in one patient who also underwent drainage of exudates. Two patients were treated by laminectomy.

Leaving aside the tumoral syndrome due to tuberculoma, the authors conclude that there are 3 fundamental indications for neurosurgical therapy in complications of tuberculous meningoencephalitis. These include (1) recent arachnoiditis that causes blocking of convexity or compression of spinal canal structures, (2) arachnoiditis localized in the posterior cranial fossa or, more often, in the spinal cord canal, and (3) hydrocephalic syndrome with intracranial hypertension.

Neurophysiologic Variants in Schizophrenia. H. V. Kamp, J. Berghorst and R. N. DeJong. A. M. A. Arch. Gen. Psychiat. 1:250-252 (Sept.) 1959 [Chicago].

Schizophrenia has been described as a basic integrative defect in the organization of stimuli coming from within and without. This is considered to be a genetically determined, biochemical, metabolic abnormality. The defect appears to be located in the region of the reticular formation, hypothalamus, thalamus, and limbic system. The metabolism here differs from that of other regions of the brain. It is more resistant to lack of oxygen and sugar and to excess of carbon dioxide. It is also more sensitive to various drugs. In this region a special system of neurons which function as a general integrating system are found. The dorsal thalamus has been considered the anatomic background for personality. The hypothalamus acts as an integrating center in the delicately balanced functioning of the autonomic nervous system. When this balance is disturbed, a homeostatic mechanism tends to restore it. Thus, it would appear that the integrative capacity of the hypothalamus could be evaluated by disturbing the balance between the sympathetic and the parasympathetic system and then appraising the homeostatic mechanism which restores it.

Methacholine (Mecholyl) chloride is a drug well suited for this study. It acts at the tissue level on the parasympathetic system and on the adrenal medulla, on the sympathetic division. It produces a change in blood pressure and pulse rate and a shifting of blood volume. The shifting of blood volume to the periphery in the systemic circulation causes flushing. This, in turn, requires an adjustment in temperature control, which, in turn, is mediated through the hypothalamus and expresses itself by sweating. Methacholine also stimulates the salivary glands. These various autonomic disturbances can be appraised clinically by noting changes in blood pressure, pulse rate, flushing, sweating, and salivation.

Methacholine was given to 150 patients on admission to hospital. Many were acutely psychotic, disoriented for time, place, and person, and very delusional and hallucinating. After the basal blood pressure and pulse rate were determined, 10 mg. of methacholine was injected into the deltoid muscle. A record was made of the blood pressure and pulse rate at 2, 5, 7, 10, 12, 15, 20, and 24 minutes. The degrees of flushing, coughing, sweating, and salivation were also recorded. These patients showed a great variation in their response to methacholine. The test was also given to 50 patients who had been hospitalized for a prolonged period and showed schizotypal deteriorations.

The clinical history of many of these patients has been reviewed 3 or 4 years after the test was given. Those who showed a marked response to methacholine left the hospital a few months after admission. The patients in this group who received insulin, psychotherapy, or tranquilizers all responded well to these forms of treatment. However, they did not improve any faster or better than those whose illness was allowed to run its natural course. They have made an acceptable social, marital, and economic adjustment. Patients who showed a moderate response to methacholine have made a marginal social, marital, and industrial adjustment. Commitment was instituted in a large number of cases. Those patients who showed a minimal reaction to methacholine have required almost continuous hospitalization. Those who showed a marked response can be described as decompensated schizoadaptive, who compensated within a few months when the precipitating stress was removed. Those who had a moderate response can be described as showing schizotypal disintegration, marked by adaptive incompetence. The stage of schizophrenia of those patients who showed a minimal response can be described as schizotypal deterioration. They constitute a vast number of the patients in mental hospitals.

Psychoses Associated with Systemic Lupus Erythematosus. J. F. O'Connor. Ann. Int. Med. 51:526-536 (Sept.) 1959 [Lancaster, Pa.].

The authors report on 39 women and 1 man, between the ages of 18 and 45 years, with systemic lupus erythematosus and with concomitant psychiatric manifestations, who were admitted to the Columbia-Presbyterian Medical Center in New York between 1950 and 1954. Fourteen of the 40 patients were considered to be essentially normal persons psychologically; their emotional problems were a normal reaction of anxiety and depression in relationship to their illness and did not warrant the attention of a psychiatrist. Five patients were psychoneurotics, with depressive reactions in 2, anxiety reactions in 2, and dissociative reactions in 1; their disturbances were subjectively related to the treatment with steroids (cortisone and corticotropin). Twenty-one patients had overt psychotic attacks during their hospitalization; of these, 11 had acute brain syndromes, and 10 had functional psychoses, with a diagnosis of schizophrenia in 7 and psychotic depressions in 3. Only 3 of the 21 patients with overt psychoses were not receiving steroids at the time of the psychotic attack. Two of the 3 had brain syndromes, and the third was considered to be schizophrenic. Fourteen of the 40 patients had neurological symptoms at some time during their illness.

As a rule, the psychosis occurred when the patient was given a higher dose of steroid than the one which had been previously required to control medical symptoms. The average amount of cortisone received before the onset of the psychosis was 190 mg. per day. The patients who had no overt symptoms of a psychiatric nature required an average dose of 100 mg. of cortisone per day. The patients in whom psychoses occurred had a severer form of systemic lupus erythematosus, which necessitated longer periods of hospitalization, and the administration of higher steroid doses was required to control the more serious medical symptoms of these patients. The psychiatric disorder might then be directly related to the severity of the disease rather than to the larger doses of steroid required. The length of the psychotic attacks ranged from hours to months. As the lupus erythematosus went into remission and the dose of steroid was reduced, all the patients recovered from their psychiatric disorders, most of them within one week. In only one patient did the psychotic reaction persist for more than 2 months after withdrawal of the steroid.

Autopsies were performed on 11 patients who died. Of these, 10 showed pathological changes involving the central nervous system, generally most intensive in the cerebrum. Such findings strongly suggest that the psychosis observed in patients with systemic lupus erythematosus is secondary to the tissue pathology. Of this group, all had either psychiatric or neurological syndromes, or both. The occurrence of a psychosis during one hospitalization did not contraindicate the reinstitution of steroid therapy. There was no evidence of alternation of medical and psychiatric syndromes; in fact, the reverse was true. The prognosis of the psychotic reactions was generally favorable. The development of a psychotic reaction is not an indication for the complete and immediate withdrawal of steroids, or for withholding steroids from those patients in whom they are medically indicated.

GYNECOLOGY & OBSTETRICS

Migraine and Eclampsia. W. N. Rotton, M. R. Sachtleben and E. A. Friedman. Obst. & Gynec. 14:322-330 (Sept.) 1959 [New York].

The authors report on 284 women with the more severe type of migraine, who had had a total of 610 pregnancies. Of the 284 women, 221 carried their pregnancies into the third trimester, and 47 (21.4%) of these, as a minimum, had some form of acute toxemia, including 15 (6.9%) who had eclampsia. This percentage was shown to be far in excess of that which could be expected by chance. Conversely, a review of 99,796 deliveries, which took place between 1922 and 1958, revealed the presence of eclampsia in 88 of the women subjected to delivery, and 18 of these had concurrent migraine, a minimum incidence of 17%, as compared with an expected incidence of 4 to 12% of migraine in the general population.

The fetal losses were surprisingly high among the pregnant women with migraine; 15 stillbirths and 13 neonatal deaths occurred among the offspring of these patients. This high perinatal mortality rate associated with pregnancy and migraine was accounted for by the increased incidence of preeclampsia and eclampsia. Two of the patients with migraine and pregnancies died, and these 2 deaths occurred in conjunction with eclampsia. Neither patient showed the classic triad of edema, albuminuria, and hypertension; one had precedent headache, and the other epigastric pain and then headache, before the onset of convulsions. Exacerbating or unchanging migraine symptoms occurring during pregnancy appear to be a particularly ominous sign, portending toxemia tendencies. The fulminating courses and the inadequacy of available therapeutic measures speak eloquently for prevention and early detection. The observation that a latent predisposition to convulsions, manifested by a migraine diathesis, may be uncovered by toxemia of pregnancy possibly signifies an association between migraine and toxemia of pregnancy.

The Optimal Time for Induction in Preeclampsia. H. M. Carey and A. W. Liley. New Zealand M. J. 58:460-466 (Aug.) 1959 [Wellington].

Examination of the salvage of premature infants, in terms of period of gestation, at the National Women's Hospital in Auckland, New Zealand, between 1954 and 1958, showed that the neonatal death rate in infants born during the 37th week did not exceed 6% and after the 38th week the risk was less than 4%. These findings suggested that there is little need to delay induction of labor in pregnant women with preeclampsia when the pregnancy has progressed beyond the 36th week. In 165 pregnant women admitted to this hospital, in whom signs of preeclampsia developed before the last month of pregnancy, the authors compared the actual results obtained by clinical management with the hypothetical results obtained by 7 different delivery schemes, all of which involve early intervention. With clinical management there were 39 intrauterine deaths and 11 actual neonatal deaths, a total loss of 50. The hypothetical results with the recommended approach (scheme 1), i. e., intervention when the calculated risk of intrauterine death first appreciably exceeds the risk of neonatal death, were 12 intrauterine deaths, 3 actual neonatal deaths, and 22 estimated neonatal deaths, a total loss of 37. Other schemes, which attempt to forestall intrauterine deaths by empirical early intervention, produce a discouragingly large increase in neonatal deaths. In pregnant women with preeclampsia, the fetal interests are best served by weighing the risk of neonatal death from prematurity against a best estimate of the risk of intrauterine death in the individual case, and by using this as a guide to the optimum time for delivery rather than relying entirely on clinical acumen or any rule of thumb.

Pulmonary Hyaline Membrane: Contamination of the Lungs by Blood-laden Amniotic Fluid in Term Infants Delivered by Cesarean Section. F. F. Snyder. Obst. & Gynec. 14:267-287 (Sept.) 1959 [New York].

The author reports on the clinical histories and complete autopsy findings of 56 infants delivered by cesarean section at term, 12 of whom were stillborn and 44 were liveborn but had died within 72 hours after the delivery. Fifteen of the 56 infants were delivered before the onset of labor, while the remaining 41 infants were delivered during labor or after an antepartum hemorrhage. The outstanding finding on microscopic examination of the lungs of the 56 infants was evidence that fetuses breathe the amniotic fluid before birth, as shown by contamination of the air passages with blood in more than 90% of these infants, and by contamination with epithelial cells and cellular debris in 32 infants. In accounting for the origin of an eosinophilic layer of amorphous matter outlining the walls of the alveoli and bronchioles, it must be borne in mind that the amniotic fluid was contaminated not only by the cells of the blood but also by the blood plasma at the time of incision of the uterus of the mother. In all 15 infants delivered before the onset of labor and before rupture of the mebranes, the air passages were contaminated with blood-laden amniotic fluid. Deaths occurred at 6 to 65 hours after delivery, and in 7 within 18 hours. In 14 of the 15 infants a layer of amorphous hyaline matter outlined the walls of many bronchioles and alveoli. Despite the briefness of the period from incision of the uterus to the first breathing of air, there was widespread contamination of the air passages by blood, revealing a hazard for the infant inherent in delivery by cesarean section.

Fetal breathing before incision of the uterus was evidenced by contamination of the air passages by foreign matter in the 12 stillborn infants who had died during labor with ruptured membranes. In these infants, erythrocytes were widely distributed in the air passages and often mixed with meconium and amorphous debris. The absence of respiratory movement at delivery limited the period of breathing of amniotic fluid to an interval preceding operative intervention. In the absence of expansion of the lungs with the entrance of air, displacement of the eosinophilic matter in a membrane-like layer along the walls of the alveoli and bronchioles did not occur. The combined effects of contamination of the amniotic fluid both during labor with ruptured membranes and during incision of the uterus were observed in 29 infants, all of whom were liveborn. In 28 of these, erythrocytes were scattered in the alveoli and bronchioles of extensive areas of the lungs. In the 7 infants who died at 15 minutes to 3 hours after delivery, little hyaline film formation was seen, while of the remaining 22 infants who died at 4 to 72 hours after delivery, extensive areas of hyaline layers were noted in 13. The frequency of hyaline membrane formation reached a peak in infants delivered before labor, rather than in those delivered during labor. Although duration of exposure to contaminated amniotic fluid was minimal in hysterotomy before labor, the reflexes and respiratory activity of the fetus were impaired less frequently at such delivery than during labor and in the presence of complications that caused fetal respiratory depression. The regular occurrence of atelectasis, in areas of the lungs showing membrane-like dispersion of the foreign matter, was further evidence of obstruction.

PEDIATRICS

Studies on the Genetic Mechanism of Cystic Fibrosis of the Pancreas. M. Smoller and D. Yi-Yung Hsia. A. M. A. J. Dis. Child. 98:277-292 (Sept.) 1959 [Chicago].

Cystic fibrosis, a generalized disease of the exocrine glands, manifests itself clinically by loss or diminution of pancreatic exocrine secretions, by increased susceptibility to upper respiratory infections and pneumonia resulting in the pathological changes of bronchiectasis, atelectasis, and emphysema, and by elevations of sodium and chloride concentration in sweat gland secretions. In addition to the major manifestations, there is evidence pointing to an increase in salivary sodium and chloride concentrations, and abnormal duodenal mucosal gland secretions. The familial nature of this disease having been described since 1946, the authors investigated the possibility as to whether more than one gene could be operative and tried to ascertain whether a clinically well heterozygous carrier could be detected.

Complete family studies were undertaken in 38 families having children with cystic fibrosis of the pancreas, and it was found that sweat sodium levels were above normal limits in about half of the parents. A similar increase was noted in one-third of the normal siblings. The data demonstrated some segregation of clinical symptoms and laboratory findings within families. However, on the limited number of families studied, one could not rule out the possibility that the variable clinical picture seen in cystic fibrosis could be the result of a single gene being modified by other genes and by environmental factors. The findings showed that the sweat sodium and chloride are directly related, that the sodium concentration was almost always greater than the chloride, and that the high sodium values had a sodium/chloride ratio close to one, but most of the lower values have a sodium/chloride ratio greater than one.

Infection of Children by Strains of Tubercle Bacilli Initially Resistant to Streptomycin or to Isoniazid. R. Debré, H. Noufflard, H. E. Brissaud and J. Gerbeaux. Am. Rev. Resp. Dis. 80:326-339 (Sept.) 1959 [New York].

The authors studied 687 strains of tubercle bacilli from children with primary tuberculosis, who were admitted to the Hôpital des Enfants Malades in Paris and the Hôpital Léon Bernard in Brévannes, France, between 1948 and 1958; 394 of these strains were isolated from patients who had not been treated with streptomycin, and 18 of these were resistant to streptomycin. Death occurred after 16 to 28 days in 6 of the 18 patients, and after 33 days and 2 months in 2. All 8 children but one had meningitis due to streptomycin-resistant organisms; they died as quickly as they would have had they received no treatment at all. The remaining 10 children made an uneventful recovery; their resistance to streptomycin became evident while they were still alert and conscious, and treatment with isoniazid and PAS was immediately started. A lag-period of 3 years has been observed in France between the time when streptomycin became available and the appearance of the first cases of initial resistance to streptomycin in untreated patients. In 1952 the incidence of infection with streptomycin-resistant tubercle bacilli increased, but since then, and coincidentally with the introduction of isoniazid, this increase has been stopped, and the overall incidence is about 5%.

A lag-phase has also been observed between the advent of isoniazid and the appearance of resistant strains in untreated children. In 1957, for the first time, 4 isoniazid strains were found in untreated patients, which were of a degree of resistance that is of clinical significance. This leads to the conclusion that the infection of nonallergic children with strains of tubercle bacilli resistant to drugs available at present is an actual fact, the clinical significance of which has now been well proved. The importance of this hazard makes it as necessary as ever to use multiple-drug therapy and to isolate patients who continue to discharge tubercle bacilli in the sputum.

Micromelia with Tetralogy of Fallot. R. H. Whittlesey. Arch. Pediat. 76:337-349 (Sept.) 1959 [New York].

The author reports on a 4-year-old boy with micromelia associated with the tetralogy of Fallot, which was present at birth. The patient was cyanotic from the time of birth. His left arm consisted of a bilobed stub protruding from the left shoulder, measuring about 2¼ in. in length and about 1 in. in diameter. After a surgical procedure a complete revelation of congenital anomalies included the following: (1) tetralogy of Fallot; (2) right-sided aortic arch and descending aorta on the right; (3) persistent ductus arteriosus; (4) absence of the innominate artery; and (5) hypogenesis of the left subclavian artery, as well as micromelia of the left upper extremity and facial dysostosis. Arching of the aorta to the right in itself is not an uncommon finding at autopsy; however, in this patient the 4 prime branchings of the aortic arch were most unusual, as was the hypoplasia of the left subclavian artery and the location of a ductus, coursing between this artery and the pulmonary vessel.

The finding of the hypoplastic left subclavian artery with the ductus arteriosus strongly suggests the possibility that these vascular abnormalities may have had more than a casual relationship to the absence deformity of the left arm. The systole of the left ventricle normally ejects blood with force into the base of the aorta, whence it is thrown around the arch to the left and directed toward the origin of the left subclavian artery. In this case, several factors were at work to prevent any large volume of blood from entering this vessel which offer the upper extremity its main supply. As blood was ejected from the left ventricle, the abnormal course of the aortic arch carried blood away from the developing ray. What blood did reach the mouth of the left subclavian artery was probably largely prevented entrance into that vessel by its small caliber. In addition, it appeared that the ductus arteriosus remained patent for a considerable period after birth, in which case a portion of the blood which did gain entrance into the subclavian artery, in spite of these features, was promptly drained off again into the pulmonary circuit. Here indeed would be ample reason for the retarded state of growth of the left upper extremity.

Activity of Glutamic-Oxalacetic Transaminase and Lactic Dehydrogenase in Cerebrospinal Fluid and Plasma of Normal and Abnormal Newborn Infants.

M. Lending, L. B. Slobody, M. L. Stone and others. Pediatrics 24:378-388 (Sept.) 1959 [Springfield, Ill.].

Determinations of glutamic-oxalacetic transaminase and lactic dehydrogenase activity in plasma and cerebrospinal fluid were performed in 20 newborn infants, between 2 and 115 hours of age, who were suspected of intracranial pathology. This group included infants whose mothers had had complicated pregnancy and delivery; infants who presented such signs as a low Apgar score, convulsions, cyanosis, or respiratory difficulty; and infants who had both of these backgrounds. A group of 54 normal infants, between 2½ and 240 hours of age, chosen at random, constituted the control in this study. Cerebrospinal fluid (2 ml.) was obtained by lumbar puncture, and plasma by femoral vein puncture, at varying age intervals. Only one spinal tap was performed, except in 3 abnormal infants who were studied again after 3 to 5 days. The specimens were stored frozen, and the enzyme activity was determined within a week, measured in units per millimeter per minute.

In the normal infants, the values of glutamic-oxalacetic transaminase activity ranged from 5 to 102 units in the plasma, with an average of 36.9 ± 18.9, and from 1 to 10 units in the cerebrospinal fluid, with an average of 4.5 ± 2.2. The lactic dehydrogenase activity ranged from 440 to 2,540 units in the plasma, with an average of 1,165 ± 543, and from 3.3 to 120 units in the cerebrospinal fluid, with an average of 32.3 ± 24. In the abnormal infants, the values for the glutamic-oxalacetic transaminase activity ranged from 16 to 76 units (average of 43.4 ± 18.5) in the plasma and from 3.7 to 15.5 units (average of 8.2 ± 2.97) in the cerebrospinal fluid; these findings show a mean increase of 82% over the normal values in the cerebrospinal glutamic-oxalacetic transaminase activity, and a mean increase of only 18% over the normal values in the plasma. The lactic dehydrogenase activity ranged from 600 to 2,540 units (average of 1,269 ± 485) in the plasma, representing a mean increase of 11% over the normal values; it ranged from 31.6 to 855 units (average of 132.2 ± 176) in the cerebrospinal fluid, representing a mean increase of 309% over the normal values.

The maternal complications and neonatal clinical status were correlated with the activities of plasma and cerebrospinal enzymes for each infant. In 19 of the 20 abnormal infants studied there was an increased cerebrospinal glutamic-oxalacetic transaminase and lactic dehydrogenase activity over that of the normal infants, although some individual overlap in the upper range of the normal and the lower range of the abnormal was observed. These findings indicate that the determination of enzymatic activity in plasma and cerebrospinal fluid may be useful in the study of newborn infants suspected of intracranial pathology.

THERAPEUTICS

Comparison of Chlorambucil and Myleran in Chronic Lymphocytic and Granulocytic Leukemia.

R. W. Rundles, J. Grizzle, W. N. Bell and others. Am. J. Med. 27:424-432 (Sept.) 1959 [New York].

The first mustard derivative suitable for oral administration was triethylene melamine (TEM), now replaced in large part by chlorambucil (CB 1348, Leukeran) which has greater chemical stability in the intestinal tract and solubility properties that favor absorption and regularity in dosage effect. In investigations carried out on the assumption that sulfonic acid and other esters might have biological effects comparable to those of the nitrogen mustards if they were to unite, also, with some cellular constituents via the ethane group (i. e., "alkylate"), it was ascertained that the sulfonic acid esters were active. Compounds with $2-OSO_2CH_3$ functional groups connected by a chain of 4 or 5 CH_2 groups effectively inhibited the growth of Walker carcinoma 256 and produced a selective neutropenia in rats. Further study of the compound with 4 CH_2 groups, busulfan (Myleran), showed it to be an effective agent in the treatment of chronic myeloid leukemia in man. The object of the present study was to compare more systematically and conclusively the effect of these 2 types of agents, with use of Myleran and chlorambucil, in patients with chronic granulocytic and chronic lymphocytic leukemia.

The effects of chlorambucil and Myleran therapy were studied in parallel in 40 patients with chronic lymphocytic leukemia and in 42 patients with chronic granulocytic leukemia. In chronic lymphocytic leukemia, chlorambucil produced good or excellent therapeutic responses in 15 of 23 patients. None of 17 patients treated with Myleran responded this well, and in 15 thrombocytopenia developed, due to adverse effects on the bone marrow. In chronic granulocytic leukemia, Myleran produced good or excellent therapeutic responses in all 21 patients treated. Only 12 of 21 patients given chlorambucil had comparable responses. Chlorambucil and Myleran appear to have relatively specific growth inhibitory effects on the lymphoid and myeloid tissues respectively. This finding should encourage further search for new alkylating groups with the possibility of discovering oncolytic agents with different tissue specificities than those presently available.

Therapy of Strongyloidiasis with Dithiazanine. J. P. Muhleisen and J. C. Swartzwelder. Am. J. Gastroenterol. 32:317-327 (Sept.) 1959 [New York].

The authors report on 32 patients with strongyloidiasis, who were treated with Dithiazanine, a new anthelmintic agent. The drug was administered in tablet form to 29 patients, and a flavored suspension was given to the remaining 3 patients. Initially, a dose of 200 mg. of the drug was given 3 times daily for 5 days. Each dose was given 2 hours after meals. Later the treatment period was extended to 21 days, because a 5-day course of therapy was inadequate to effect a cure. Once the 21-day course was shown to be adequate, the dosage was reduced from 600 to 300 mg. per day, without loss of therapeutic efficacy. Diagnostic forms of Strongyloides stercoralis were not demonstrable after therapy in the feces and duodenal drainage aspirates of 29 of the 32 patients. The infection thus was eliminated in 90% of the patients. The side-reactions to therapy were infrequent, mild, and evanescent. Autopsy was performed on 2 patients who died of causes unrelated to the therapy. Thorough examination of the upper small intestine revealed no parasites, thus providing additional and conclusive evidence of eradication of the infection.

PATHOLOGY

Anterior Tibial Syndrome Due to Arterial Embolism and Thrombosis: Ischaemic Necrosis of the Anterior Crural Muscles. B. J. Freedman and C. H. R. Knowles. Brit. M. J. 2:270-275 (Aug. 29) 1959 [London].

The authors report on 5 patients with anterior tibial syndrome, 2 cases being due to embolism, 1 to thrombosis after hemorrhagic shock, and 2 to thrombosis associated with senile atherosclerosis. The main features of the syndrome are ischemic necrosis of the tibialis anterior muscle and, in greater or less degree, of the extensor hallucis longus and extensor digitorum longus muscles; these 3 muscles occupy the rigid-walled anterior tibial compartment. The immediate cause of the syndrome is occlusion of the anterior tibial artery or its parent trunk. This may be due to (1) swelling of the muscles after unaccustomed exertion, and consequent rise in intracompartmental pressure above the arterial blood pressure; (2) local expanding lesions within the compartment, with similar effect; and (3) embolism or thrombosis of the anterior tibial artery or its parent trunk.

In the first patient, pulsation was present in the posterior tibial artery and absent from the dorsalis pedis artery, indicating a block in the anterior tibial artery. All muscles within the compartment were paralyzed. Biopsy on the 11th day showed ischemic necrosis. The specimen taken 14 months later showed evidence of regeneration. The electrical reactions on the 35th day indicated neuropathic paralysis of those muscles which had not undergone necrosis. The return by the 60th day of contractility and faradic response to the greater part of the muscle group is attributable to recovery from the neuropathy and to regeneration in some of the necrotic muscle fibers. At the onset, transient pain was complained of in the opposite leg.

In the second patient, pulsation was absent from the posterior tibial and dorsalis pedis arteries on the affected side, indicating a block, clinically embolic, of the popliteal artery or its bifurcation; yet evidence of ischemia was confined to the specially vulnerable muscles of the anterior crural group. The case of the third patient, in whom the syndrome was ascribed to thrombosis, was remarkable for the liquefaction undergone by the contents of the compartment. As the skin overlying the compartment was not infected, the infection within was probably derived from one of the patient's many boils. No other foci were found. It was puzzling to see how blood-borne organisms could have reached an avascular region. Possibly they were in transit at the moment of infarction. Although arterial thrombosis presumably occurred on a basis of atherosclerosis, infarction was precipitated by profound anemia and oligemic shock.

The 4th and 5th patients were advanced in age and presented cerebral and cardiac signs indicating the presence of widespread and severe atherosclerosis. Arterial thrombosis was the immediate cause of the syndrome in these patients. A slowly progressive ischemic atrophy and fibrosis, seen histologically, gave rise to no clinical signs. Despite the failure of limited medical measures in the 4th and 5th patients, the authors suggest that the simultaneous administration of papaverine, nylidrin hydrochloride, and anticoagulants may offer hope of resolution in cases due to arterial thrombosis or embolism.

BOOK REVIEWS

Aviation Medicine: Selected Reviews. Edited by Clayton S. White, W. Randolph Lovelace II, and Frederic G. Hirsch. AGARDograph no. 25. Cloth. $12. Pp. 305, with illustrations. Published for and on behalf of Advisory Group for Aeronautical Research and Development, North Atlantic Treaty Organization, by Pergamon Press, Inc., 122 E. 55th St., New York 22; 4 & 5 Fitzroy Sq., London, W. 1, England; 24 rue des Écoles, Paris 5e, France, 1958.

This book contains reports by 12 scientists who reviewed selected topics and assessed recent advances in the instrumentation, methodology, and analytical techniques of interest in aviation medicine culled from many publications, over 700 of which are cited as references. Their aim was to document condensed sources of information summarizing specialized portions of the aeromedical and related sciences. While great emphasis was directed to respiratory physiolgy and metabolism, the papers cover a wide range of subjects of interest not only to physicians in aviation medicine but also to other scientists who need a condensed guide to specialized sources of data. This book should be a valuable reference manual to all aerospace medical research scientists. Some parts are highly technical and will be appreciated chiefly by research and laboratory workers. The editor has included in his introduction brief summaries of each paper.

These papers deal with spirometric methods, high-speed motion picture photography as an aid in biomedical investigation, measurement of atmospheric ozone, methods and apparatus for the study of stress reactions and metabolic changes, dosimetry of ionizing radiations, technical developments applicable to problems in pathology, temperature measuring techniques for physiological research in aviation, analysis of respiratory gases, aerosols, transducers, spectrometric methods, and gas sampling methods. There is an excellent index and the many illustrations are well chosen. The book is highly recommended for every laboratory and aviation medical library.

Difficult Diagnosis: A Guide to the Interpretation of Obscure Illness. By H. J. Roberts, M.D. Cloth. $19. Pp. 913, with 99 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

This extraordinary book was written by a single author who is a consultant in private practice and not presently identified with any teaching institution. He accomplishes completely what he sets out to do, presupposing a good grounding in ordinary textbook medicine on the part of the reader but not attempting a schematization of differential diagnosis. Part 1 contains groupings of diseases frequently producing puzzling symptoms and part 2 a classification and analysis of useful diagnostic procedures. The atlas is a separate section of black and white and colored illustrations of dermadromes. Bibliographies are given separately for each part. There is one index for signs, symptoms, and laboratory manifestations and another for general topics.

Part 1 is something of a hodgepodge, but this is inevitable because of the author's intention. Numerous cross-references within the book and references to original articles serve to mitigate this fault. At first glance the book seems to overstress the rare and unusual but, as the author says, the finished diagnostician needs to be exposed to these if he is to bear them in mind in a difficult case. The large number of syndromes considered under eponymic labels is distressing, but there is no ready substitute for this usage. Some chapters are better than others, as might be expected when such an enormous field is encompassed by one author. Part 2 on the whole represents a judicious choice of tests and procedures with what appears to be a well-balanced appraisal and presentation. The illustrations in the atlas of systemic dermadromes are well selected and reproduced. Technical considerations probably prompted the author to use the atlas device rather than to disperse the pictures in appropriate places in the text, and this causes only minor inconvenience. The candidate for board certification, if he reads part 1, will at least have heard of nearly all of the footnote questions which might confront him. The internist should find all of the book useful, and especially part 2 as a reference to unusual tests and procedures. It should be valuable to teachers of medicine and perhaps other specialties. Investigators may find the bibliographies alone worthwhile.

The History of Nursing: An Interpretation of the Social and Medical Factors Involved. By Richard H. Shryock, Ph.D. Cloth. $5. Pp. 330. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

This book should prove of great value to persons interested in the education of nurses, as well as to student nurses themselves. The author traces the various stages of nursing from its early or primitive period to the present. He shows the interrelationship between medicine and nursing and discusses the social and scientific background of nursing. The material is well organized and has good continuity. Perhaps more information should have been included concerning modern trends; many new fields are now open, whereas during earlier periods nurses were principally engaged in bedside nursing. One other matter which might have been mentioned is the attempt being made by unions to organize this profession.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

CENTRAL SCOTOMAS

To the Editor:—*Do retrobulbar neuritis or optic atrophy cause central scotomas?*

Heino Trees, M.D., Washington, D.C.

Answer.—The loss of vision characteristic of central scotomas is limited to the area of the visual field which corresponds to the point of fixation, i. e., the macula. This is due to involvement of the maculopapillar bundle, which is highly susceptible to toxins and pressure. Central scotomas frequently are seen in patients with toxic amblyopia, multiple sclerosis, and retrobulbar neuritis. Thus, central scotomas may arise from either retrobulbar neuritis or in the course of a developing optic atrophy.

CAUSE OF CHEILOSIS

To the Editor:—*The answer to the question about cheilosis in a 76-year-old man, in* The Journal, *Aug. 29, page 2266, is open to comment. In the United States, where people are relatively well nourished, vitamin deficiency as a cause of cheilosis should be considered last, not first, except with patients who are alcoholics or food faddists or those having deficiency in absorption from the gastrointestinal tract. Angular stomatitis is more likely due to a narrow bite, which can be corrected by prescription of proper dentures. Cheilosis may be due to prolonged exposure to the sun's rays, resulting in chronic actinic dermatitis. The treatment includes observation for premalignant and malignant lesions and protection from sunlight, primarily by use of a sun screen ointment.*

Ira Leo Schamberg, M.D.
7852 Montgomery Ave.
Elkins Park, Pa.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Dr. Schamberg indicates that vitamin deficiency should be considered only in alcoholics, food faddists, and those with deficiency in absorption from the gastrointestinal tract. Information in the query provides no indication that the patient is not an alcoholic, nor does it exclude the possibility of deficient absorption. Trophic or other irritative changes were mentioned. My reply stated "Not all the categories of causes of cheilosis are known." If a narrow bite is the main cause of angular dermatitis, it would be worthwhile to know whether this particular patient has a narrow bite and improper dentures, before making such a diagnosis. Cheilosis is, at times, due to prolonged overexposure to the sun's rays. The physician making the comment apparently has a simple explanation for both cheilosis and angular stomatitis; I do not.*

INTRACTABLE TRICHOMONIASIS

To the Editor:—*I wish to comment on "Intractable Trichomoniasis," in* The Journal, *Sept. 19, page 373. The crux of the answer is that trichomonads do not thrive in the flora of a normal vagina. They occur as harmless parasites throughout the animal kingdom. In the human host their presence may cause psychic effects, but any other symptom would be due to some underlying abnormality. (Moench,* M. Rec. *150:83 [Aug. 2] 1939;* Arch. Ther. *p. 425 [Dec.] 1926.) These studies give examples demonstrating these concepts. One patient had erosion of the cervix and no trichomonad infestation until after cauterization of the cervix had been done. When the cervical discharge disappeared, the trichomonads appeared also. Another patient had an infestation in which every type of treatment used produced only a temporary response. Later, because of the patient's increasing nervousness, a basal metabolism test was done and showed hyperthyroid function of a toxic nature. After an operation for the hyperthyroidism the trichomonads were eliminated.*

G. L. Moench, M.D.
27 W. 55th St.
New York.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*I agree that patients should have a thorough evaluation, not just regionally but totally; this point I had taken for granted. There should be special observations for abnormal conditions in the vagina, urethra, bladder, vaginal submucosa, and gastrointestinal tract. Occasionally a marriage partner may be a carrier.*

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

WASHINGTON NEWS

Rayburn Predicts Social Security Vote . .
More Active Federal Medical Role Urged . .
Poliomyelitis Count . .
Food Additives . .
Drug Hearings . .

SOCIAL SECURITY LIBERALIZATION SEEN

House Speaker Sam Rayburn (D., Texas) predicted that Congress this year would approve a liberalization of the social security program. He said that cash benefits may be increased and flatly forecast approval for elimination of the 50-year age requirement for permanently and totally disabled persons under the program.

However, the veteran lawmaker did not mention the controversial Forand bill that would expand the social security program to include partial health care for elderly beneficiaries through higher social security taxes.

Rayburn made the statements at a news conference as Congress opened the second half of its 86th session.

Meanwhile, a year-end report showed that benefits paid out under the social security program since its inception in 1940 have totaled 50.4 billion dollars and have gone to some 21 million persons.

William L. Mitchell, Commissioner of Social Security, said checks will be mailed in January to 13,700,000 beneficiaries, an all-time high. The original social security tax was 1% on a worker's first $3,000 of income, with the employer matching this. On the first of this year, the tax rose to a new high of 3% on the first $4,800 of income, and under already scheduled step increases will reach 4½% by 1970. The self-employed will have to pay even more.

Mitchell said the old age and survivors trust fund was estimated at 20.1 billion dollars as of Dec. 31, 1959. In addition there was 1.9 billion dollars in the disability insurance trust fund.

WELFARE GROUP URGES MORE ACTIVE FEDERAL MEDICAL ROLE

A federal advisory committee of social welfare experts urged stepped-up government programs to improve health care for indigent persons. "Since it appears that future public welfare costs may increase, largely because of increasing medical care needs and costs, federal and state governments, in cooperation with nongovernmental agencies, should take a more active role in stimulating more comprehensive medical services of high quality, including preventive services," said the committee in a report to Congress and the Department of Health, Education, and Welfare.

The Advisory Council on Public Assistance report was based on a year-long review and analysis of the financial operations of public assistance in relation to the old age, survivors, and disability insurance program, the fiscal capacities of the states and federal government, and other aspects of public assistance. The 12-member committee, named by HEW Secretary Arthur S. Flemming, was established by Congress in 1958. Most of the recommendations concerned financial aspects of the federal-state program to aid the blind, dependent children, indigent aged, and permanently and totally disabled.

All levels of government, according to the report, should take steps "toward assuring that health services available to public assistance recipients are comprehensive in nature and of high quality. Improvements in medical care should not be accomplished by reducing money payments to recipients."

"The federal government should exercise greater leadership in stimulating and encouraging states to extend the scope and content and improve the quality of medical care for which assistance payments are made to or on behalf of needy individuals. As specific steps toward this end, we recommend federal leadership in (1) developing guides to states for evaluation and moving toward improving their programs of medical care; (2) requiring periodic state reports on types and amounts of medical care for which assistance is paid; and (3) publishing periodically comparative state data secured from these reports and other information that will promote greater public understanding about needed medical care."

The committee also recommended establishment of a "broadly constituted" medical care advisory group to assist HEW "on all aspects of medical care in public assistance."

The group also proposed that the 50-year age requirement be dropped from the program for permanently and totally disabled persons. The administration had previously supported such a move.

Other recommendations included (1) establishment of a national institute "with responsibility for carrying on research studies and demonstration projects leading to a strengthening of family life" and (2) "Extension of social insurance to the fractional segment of the labor force not presently covered by any public retirement system, and particularly to more farm and household workers."

The Administration, of course, is not required to adopt the proposals, which are merely advisory.

Members of the committee are Social Security Commissioner William L. Mitchell, Chairman; Frank Bane, consultant to the director, Office of Civil and Defense Mobilization, Washington, D. C.; Harry A. Bullis, former chairman of the board, General Mills, Inc., Minneapolis; John E. Burton, vice-president, Cornell University, Ithaca, N. Y.; Wilbur J. Cohen, professor of public welfare administration, University of Michigan, School of Social Work, Ann Arbor, Mich.; Miss Loula Dunn, director, American Public Welfare Association, Chicago; Mrs. Katherine Pollak Ellickson, assistant director, Department of Social Security, American Federation of Labor and Congress of Industrial Organizations, Washington, D. C.; Raymond W. Houston, commissioner, New York State Department of Social Welfare, Albany, N. Y.; Bernard Lander, associate professor of sociology, Hunter College, New York, and chairman, commission of family and youth welfare of the Synagogue Council of America; William R. MacDougall, general counsel and manager, County Supervisors Association of California, Sacramento, Calif.; William H. Robinson, chairman, Illinois Commission on Public Aid and Assistance, Chicago; Charles J. Tobin Jr., secretary, New York State Catholic Welfare Committee, Albany, N. Y.; and Rev. William J. Villaume, executive director, department of social welfare of the National Council of Churches of Christ, New York.

INCIDENCE OF POLIOMYELITIS IN 1959

The final report of 1959 showed 8,531 cases of poliomyelitis, compared with 5,987 during 1958. The Public Health Service reported that there were 69 cases of poliomyelitis during the final week of last year, compared with 85 during the same span a year earlier.

Of the 1959 total, 5,661 of the cases were paralytic, while 3,090 paralytic cases were reported in 1958.

Texas ranked first in the incidence of poliomyelitis last year, with 530 cases. New York followed, with 523 cases.

PHS noted that the higher 1959 poliomyelitis rate did not indicate lack of efficacy of the Salk vaccine, since the bulk of the cases occurred in unvaccinated persons. It has urged vaccination drives at the community level before the summer poliomyelitis season. A high proportion of the 1959 incidence involved low-income groups in crowded city neighborhoods. Young adults also represented a sizeable percentage.

FOOD ADDITIVE BAN MODIFIED

The Food and Drug Administration allowed food processors and chemical companies to apply for extensions for the use of chemical additives that otherwise might be banned. Under present law, these firms must prove by March 6 that additives used in food are safe and harmless or remove them.

FDA said companies which have not yet submitted such proof may submit requests for extensions beyond the March 6 deadline to use the additives. The agency warned that it would be illegal to use any additives after that date that have not either been proved safe or been granted an extension.

Extensions will be granted, FDA said, only if "no undue risk to the public health" is involved.

Under the new law going into effect, food processors and chemical concerns must provide the government with satisfactory proof that additives used to color, enrich, preserve, or flavor food or cosmetics are safe. Previously, the burden of proof was on the government, and litigation was often required to bar the use of possibly harmful substances.

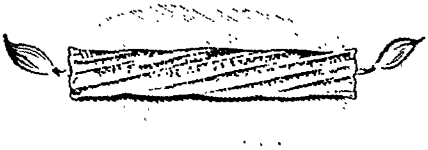
Meanwhile, the agency declared that 37 additional additives used in animal feeds have been classified safe by a panel of several hundred scientists. So far, of about 1,000 chemical substances used in food and cosmetics, about 200 have been determined harmless. Of the remainder, private companies have submitted only 70 additives for clearance. HEW Secretary Arthur S. Flemming has stated that it appeared likely some additives will be automatically barred by March 6 because of failure to submit proof of their safety.

DRUG PRICE HEARINGS

A second round of hearings on drug prices was scheduled to start during the week of Jan. 21 by the Senate antitrust subcommittee headed by Sen. Estes Kefauver (D., Tenn.). Top officials of four large companies that produce tranquilizers were summoned to testify. In November, the subcommittee questioned makers of drugs used for treatment of arthritis.

MISCELLANY

Nine grants totaling $321,894 were awarded by the U. S. Public Health Service to support community cancer demonstration projects. The nine projects were recommended for approval by the Advisory Committee to the Cancer Control Program and the National Advisory Cancer Council. Five of the projects will deal with tumor records and registries, two will screen large numbers of women for cancer of the cervix, and two will further education in cytology, the science of cells. The purpose of the studies is to shorten the interval between discoveries in research and the application of these findings at the community level. They are the first to be assigned from the $1,500,000 appropriated by Congress for this purpose during the current fiscal year.



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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1960

January

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 11-13. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, North Carolina Chapter, Hotel Barringer, *Charlotte, N. C., Feb. 26-27. For information write Dr. Alex*ander Webb Jr., 201 Bryan Bldg., Cameron Village, Raleigh, N. C.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

American Academy of General Practice, Philadelphia, Mar. 1 Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 1 Executive Director.

American Association for the History of Medicine, Inc., Charl S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Insti Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broa Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Fo Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., U Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Ma Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Trea

American Laryngological Association, Deauville Hotel, Miami B Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of T nology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Soc Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. St Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minne 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Dea Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Ba Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, real, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory versity, Atlanta 22, Ga., Secretary.

Intermountain Pediatric Society, Stardust Hotel, Las Vegas, Mar. 28-29. Dr. Joseph R. Newton, 2000 S. 9th East, Salt Lake Utah, Publicity Chairman.

Missouri State Medical Association, Sheraton-Jefferson Hote Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. L Executive Secretary.

National Health Council, National Health Forum, Miami Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, tive Director.

National Multiple Sclerosis Society, New York City, Mar. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Ma Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltim Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave. Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Ex Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahom Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral S Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jacks Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Ex Secretary.

American Association of Anatomists, Statler-Hilton, New Yor Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Me Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, Chicago, Apr. 11- Calderon Howe, Columbia Univ. College of Physicians and Su New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman, of Pathology, L. S. U. School of Medicine, New Orleans, La., Se

American Association of Railway Surgeons, Drake Hotel, C Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chica Executive Secretary.

American College of Obstetricians and Gynecologists, Net Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardson, Monroe St., Chicago 3, Executive Secretary.

American College of Physicians, Mark Hopkins & Fairmont, San cisco, Apr. 4-9. Mr. E. R. Loveland, 4200 Pine St., Philadel Executive Secretary.

American College of Surgeons, Sectional Meeting, Hotel Leam Minneapolis, Apr. 11-13. For information write: Dr. H. P. Sa 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Kahler Rochester, Minn., Apr. 14. For information write: Dr. H. P. Sa *40 E. Erie St., Chicago 11.*

American Dermatological Association, Inc., Boca Raton Hotel Raton, Fla., Apr. 8-12. Dr. Wiley M. Sams, 308 Ingraham Bldg., 32, Fla., Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. D.Sc., 9650 Wisconsin Ave., Washington 14, D. C., Executive Se

American Proctologic Society, Shamrock Hilton Hotel, Houston, Apr. 25-27. Dr. Norman D. Nigro, 10 Peterboro, Detroit 1, Se

American Public Health Association, Southern Branch, Me Tenn., Apr. 13-15. Dr. L. M. Graves, Shelby County Health ment, Memphis, Tenn., Chairman, Local Arrangements Comm

(Continued on page 30)

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CARDIAC ENLARGEMENT DUE TO MYOCARDIAL DEGENERATION OF UNKNOWN CAUSE

PRELIMINARY REPORT ON EFFECT OF PROLONGED BED REST

George E. Burch, M.D.
and
John J. Walsh, M.D., New Orleans

The therapeutic value of prolonged, strict bed rest in cases of severe myocardial degeneration was studied in five patients. In each case, signs of congestive heart failure had persisted despite conventional management. The bed rest and hospital care, specifically designed to minimize the work requirements of the patient's heart, were then added to the regimen. Two patients returned to their normal activities after 10 to 13 months of care in the hospital. At the time of writing three patients were still in the hospital, but their prognosis had been changed from poor to fair. Cardiomegaly had been present in each case before the rest program was instituted, and reduction of cardiac size was an essential criterion of improvement.

RECENT advances in therapy have tended to render uncertain the efficacy and desirability of prolonged bed rest in various disease states. This is particularly true in cardiovascular conditions in which the *sine qua non* of successful therapy once included continued bed rest as much as it did digitalis. So successful have been the effects of the newer diuretic, antihypertensive, and cardiotonic preparations on many aspects of the manifestations of cardiac disease that continued bed rest is greatly neglected, even in patients with rheumatic heart disease. To this development must be added the general lack of a tradition of prolonged bed rest in cardiovascular diseases, other than rheumatic fever, to the degree that such a tradition exists mainly in phthisiology. Thus, neither the patient nor the physician accepts with equanimity the therapeutic approach which includes strict bed rest for periods up to one year or longer. Yet our experiences with such programs, when applied to patients suffering from nonrheumatic myocarditis of various types, were sufficiently satisfying to warrant this preliminary report.

For some time the problem of nonrheumatic myocarditis and the markedly dilated heart which failed to respond to conventional therapy has concerned us. As we proceeded further into this complex field, we became more impressed with the multiplicity of factors which can cause myocarditis or myocardial degeneration with generalized cardiac dilatation. We are also impressed with our lack

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From the Tulane Medical School, the Charity Hospital of Louisiana, and the Research Laboratory, U. S. Public Health Service Hospital.

of knowledge of the causes and basic physiological alterations in any specific case. Yet the clinical picture and course of the myocardial damage, whatever the etiological background, is essentially uniform.

Our concern has been principally directed to those typically young patients with severe, seemingly irreversible cardiomegaly, who follow a progressively downhill course, dying from cardiac insufficiency, embolization, or abrupt rhythm disturbances, usually within 2 to 12 months after the onset of illness. This dismal outcome occurs in spite of all conventional forms of therapy, and usually after several brief periods of hospitalization, each of which is characterized by definite but limited response to therapy and by an obvious progressive deterioration of the patient's condition. In another group of these patients the course is protracted over several years but is otherwise essentially the same as that of those who live for shorter periods of time. Recognizing the failure of the usual forms of therapy and convinced of the virtues of rest, we have undertaken to investigate the value of prolonged bed rest in the therapeutic regimen of the patient with the persistently dilated heart. This report is concerned with a preliminary description of what appears to be extremely promising results.

Methods

From a group of patients in whom the diagnosis of idiopathic generalized myocardial dilatation had been made, five patients were selected only because of their incomplete responses to conventional therapy, as manifested by persistent severe cardiomegaly, and their willingness to participate cooperatively in this therapeutic program. Each showed marked reduction in cardiac reserve, although symptoms were not necessarily severe while the patient was at bed rest. The patients were placed in a special metabolic unit and their conditions maintained on therapy with strict bed rest, in addition to the usually accepted forms of therapy used for chronic congestive heart failure. Initially bathroom privileges were limited to the use of a bedside commode. As improvement occurred, the patients were permitted to ambulate only to the extent of using a lavatory immediately adjoining the unit.

The units were air-conditioned for comfort. The maintenance of a cool comfortable environment was believed to be of extreme importance, since the principal objective of therapy was the reduction of cardiac work to an absolute minimum. Previous studies have clearly demonstrated the effect of a hot and humid environment in increasing cardiac work, cardiac output, and stroke volume.[1] Therapy in all other respects was identical to that used in these patients prior to inclusion in the special study group and to that used on the medical service of a university hospital. In an effort to keep the patients contented during the long period of institutionalization, television, occupational therapy, selective diets (salt restriction as indicated), and social services were used.

Considerable emphasis must also be placed on the importance of adequate nursing services. Patients and physicians alike tend to resist chronic hospitalization and prolonged bed rest. It is only through the combined efforts of all ancillary services that the patient can be benefited by such a therapeutic program. Mental rest, of importance equal to physical rest, can be obtained only with the aid of social, occupational, and physiotherapy services, in conjunction with complete nursing care.

Report of Cases

Case 1.—In December, 1955, about five months after her ninth pregnancy, a 27-year-old woman was hospitalized because of severe congestive heart failure, which was followed in two weeks by an upper respiratory infection. A diagnosis of "myocarditis" was made, and the patient was treated with digitalis, diuretics, and a low-salt diet. Thereafter, she remained well until about three months after her 10th delivery, when she again noted the onset of symptoms of congestive heart failure. She was admitted to the hospital in July, 1958. Examination at that time revealed normal blood pressure, severe congestive heart failure, marked cardiomegaly, hepatomegaly, and protodiastolic gallop rhythm. Although each of her pregnancies had been complicated by "high blood pressure," she apparently became normotensive after each delivery. Extensive diagnostic studies again failed to reveal the cause of her cardiac disease.

The patient was admitted to the special newly created metabolic ward for prolonged bed rest therapy. Treatment consisted of strict bed rest, diuretics, salt restriction, and digitalization. Initially, treatment was complicated by marked sensitivity to digitalis; this sensitivity subsequently disappeared when the patient recovered. Progress was slow, and the diastolic gallop rhythm persisted for more than eight months. Coincidental infections with Ascaris lumbricoides and Endamoeba histolytica were treated without difficulty. The patient showed gradual improvement during her 13 months of hospitalization and strict bed rest (fig. 1) and was discharged. She has returned to normal activities on therapy with maintenance doses of digitalis.

Comment.—For the first time since the onset of her cardiac disease several years previously, not only was she free from symptoms and signs of congestive heart failure but her heart had returned to normal size. Her condition was much improved physically and mentally at the time of discharge from the hospital. The patient was instructed to avoid physical and mental stress and fatigue to reduce the likelihood of recurrence of the cardiac ilatation. The duration and stability of the cardiac improvement are yet to be determined by close follow-up.

The prolonged bed rest during this period of hospitalization differed from that previously used in that it was closely supervised and enforced and its potential benefits were emphasized to the patient. he benefits are gradually developed and must be accumulated. Patience and determination of purpose on the part of the doctors and the patient are paramount, if success is to be achieved.

Case 2.—A man was first found to have congestive heart failure early in 1957 when he was 39 ears of age. No etiological basis for the cardiac disease could be found. During the next two years, he was treated as an inpatient and as an outpatient with salt restriction, intermittent short periods of incomplete bed rest, and digitalis. Response to therapy was unimpressive, with progressive disability and cardiomegaly. He was rehospitalized in February, 1959, because of severe congestive heart failure with marked cardiomegaly. Once more diagnostic studies revealed no obvious cause for the cardiac disease.

The patient was admitted to our special metabolic ward, treated with strict bed rest, salt restriction, and diuretics. Digitalization was effected and maintained. The diastolic gallop rhythm, present on admission, disappeared after several weeks. Since admission, the patient has shown progressive improvement, although he did experience one episode of auricular fibrillation, which rapidly responded to quinidine therapy. The patient, at the time of this writing, is entering his seventh month of hospitalization. It is anticipated that, provided improvement continues, he will be discharged to outpatient status within three months when his heart has returned to normal size (fig. 2).

Comment.—Like the first patient, this man improved gradually but progressively. His heart returned to a normal size, and he became free from symptoms and signs of cardiac disease. The only point of difference from previous therapy for this patient was the use of the strict bed rest for a prolonged period. This patient and the other patients became so impressed with the improvement in their cardiac status that it became progressively less difficult to convince them that they should remain in bed.

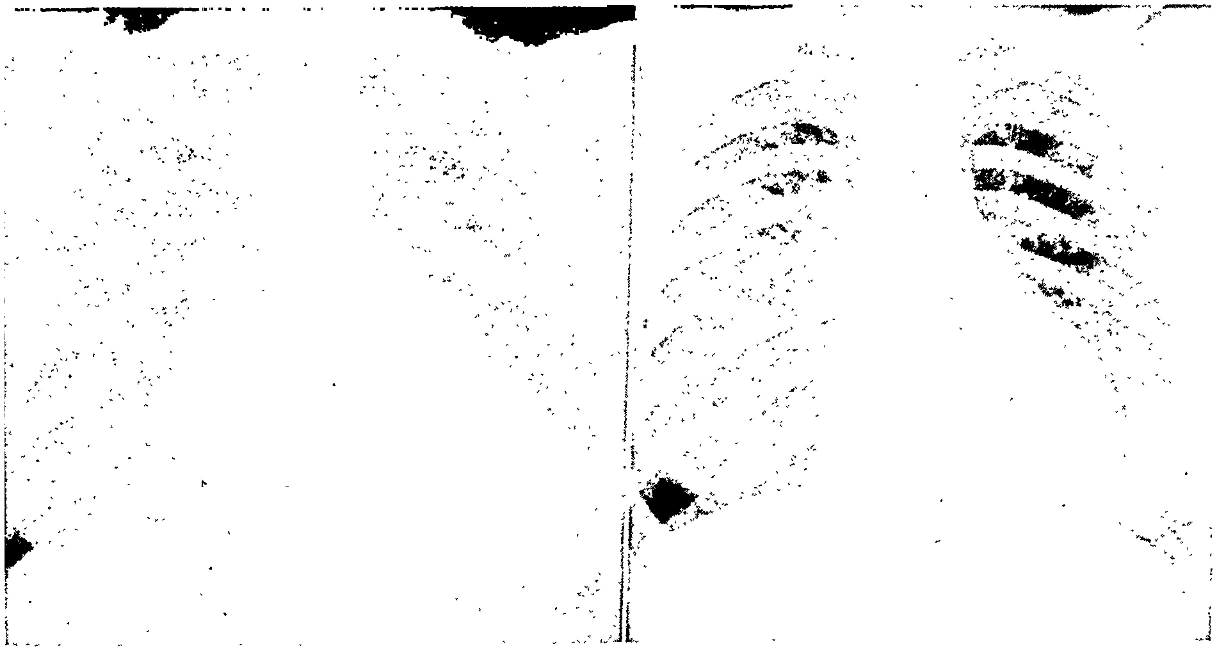

Fig. 1.—Chest roentgenograms of patient taken, *left*, at beginning and, *right*, on completion of 13 months of bed rest.

Case 3.—In 1937, at 24 years of age, a woman was subjected to a subtotal thyroidectomy because of thyrotoxicosis. She was well until the middle of 1957 when she once more developed the signs and symptoms of thyrotoxicosis and was found to have a radioiodine uptake of 55%. After she had been given therapy with methimazole (Tapazole) for nine months, a nodule was removed from the thyroid, after which all evidence of thyrotoxicosis disappeared. However, three months prior to this operation the patient had been hospitalized because of severe congestive heart failure. The tentative diagnosis was thyrotoxic heart disease. She responded to rest, diuresis, and digitalization, but considerable cardiomegaly persisted. In October, 1958, about six months after thyroid surgery, she was again hospitalized because of severe congestive heart failure, marked cardiomegaly, protodiastolic gallop rhythm, and hepatomegaly. There was no obvious cause for her heart failure. With intermittent rest, diuresis, and digitalization, the symptoms of heart failure disappeared, although the cardiomegaly and gallop rhythm persisted.

The patient was admitted to our special metabolic ward and maintained on therapy with strict bed rest for a period of 10 months. During the first six months of this period, the gallop rhythm and sensitivity to digitalis persisted. Difficulties were encountered in controlling severe heart failure because of exaggerated response to digitalis preparations. However, during the last four months of hospitalization her condition rapidly and progressively improved so that she was ultimately allowed to resume her normal activities; maintenance doses of digitalis continued to be given.

Comment.—This patient also showed marked improvement, with reduction of her cardiac size to normal (fig. 3). She showed, however, as apparently is to be common experience, that it is necessary to expect a slow reduction in cardiac size at first, and this period of watchful waiting may last six or more months. With patience and determination of purpose, the efforts will be rewarded with fairly rapid improvement once it begins. By careful and frequent follow-up examinations, it may be determined whether therapy with bed rest should be reinstituted.

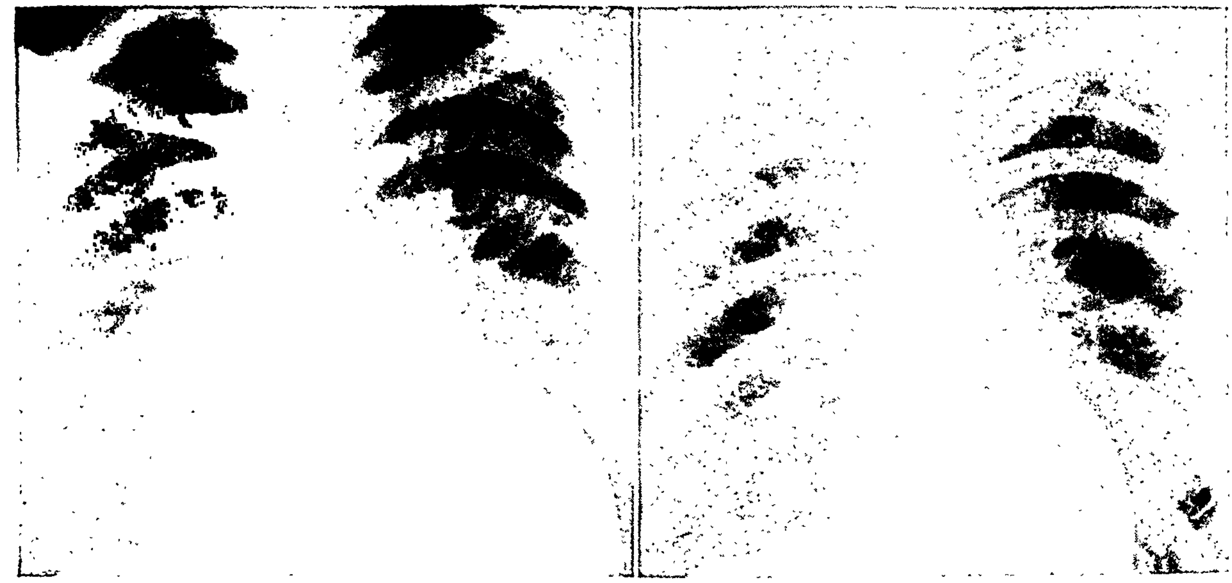

Fig. 2.—Chest roentgenograms of patient taken, *left*, at beginning and, *right*, on completion of 7 months of bed rest.

Case 4.—Beginning in January, 1959, a 15-year-old boy noted the onset of frequent episodes of abdominal distress of a cramping nature in conjunction with increasing exertional dyspnea and easy fatigability. In March, 1959, these symptoms became so severe as to necessitate hospitalization. Examination at that time revealed marked cardiomegaly. There was a moderately loud soft blowing systolic murmur confined to the mitral area. With the exception of bilateral basal rales, the remainder of the examination was not remarkable.

The patient was admitted to the metabolic ward for prolonged bed rest therapy. Although he responded to digitalization, his first three months of hospitalization were complicated by recurrent episodes of supraventricular tachycardia, always controlled with quinidine and reserpine. During this same period he manifested undue sensitivity to various digitalis preparations. Subsequently, he improved considerably and became asymptomatic. After six months of hospitalization he continued to exhibit marked tachycardia on exertion, a lessened sensitivity to digitalis-like drugs, and decreasing cardiomegaly. An additional period of hospitalization for three to six months is contemplated at the time of this writing. It should be noted that at no time have we been able to elicit historical or clinical evidence of rheumatic fever. Results of numerous determinations of the sedimentation rate, C reactive protein level, and antistreptolysin titer have always been within normal limits. Many throat cultures have failed to reveal the presence of streptococci. The systolic murmur has become almost inaudible.

Comment.—After the expected initial lag in response to therapy, the patient began to show improvement, which, once established, progressed rapidly. The patient will continue with bed rest until it is believed safe to allow ambulation. It appears that he would not have improved without rest and might even have died, since he was extremely ill and his condition was progressively deteriorating.

Case 5.—A 29-year-old woman, whose first pregnancy and delivery had been uneventful, first developed symptoms of congestive heart failure in the spring of 1956, during the fifth month of her second pregnancy. These symptoms consisted primarily of edema and dyspnea and were associated with an elevation of her blood pressure to an unknown level. Delivery was uncomplicated and the blood pressure level returned to normal. A third pregnancy was uneventful and terminated in spontaneous delivery at term in December, 1957. She apparently did not exhibit hypertension or other abnormalities during the last pregnancy. Beginning between three and four months after the last delivery she developed progressive dyspnea, edema, and orthopnea. Examination at that time revealed cardiomegaly, normal I^{131} uptake, and a blood pressure of 130/100 mm. Hg. The electrocardiogram indicated left ventricular hypertrophy. Digitalization was effected with good relief of symptoms, but subsequently the patient discontinued taking medicaments. Her symptoms began to return after several weeks. In July, 1958, she was hospitalized for severe congestive heart failure. Admission to the hospital was precipitated by a pulmonary embolism. The latter was associated with typical clinical, roentgenographic, and electrocardiographic findings.

The patient was admitted to the special metabolic ward for prolonged therapy with bed rest. Treatment consisted of digitalization and administration of diuretics, oxygen, and anticoagulants. Brief courses of steroids were given empirically and without obvious effect. Undue sensitivity to the effects of digitalis-like preparations complicated treatment during the first six to eight months of hospitalization. A combination of severe emotional disturbance and small veins made anticoagulant therapy almost impossible. At times the patient absolutely refused to permit the taking of blood samples. On at least two occasions she experienced additional pulmonary emboli and a probable splenic infarction on another occasion. These three catastrophes occurred during periods of inadequate anticoagulant therapy. On numerous occasions this patient appeared moribund. Two episodes of psychotic behavior complicated the situation. Over a period of 13 months of continuous hospitalization she had a persistent diastolic gallop rhythm. During the first nine months of therapy, her heart was in almost constant failure and showed no reduction in cardiomegaly. However, thereafter, her condition progressively improved. For the first time her heart showed definite reduction in size which appeared to be progressive. Although the reduction of heart size is very limited, further improvement is anticipated. All diagnostic studies have failed to reveal the etiological basis for her heart disease.

Comment.—This patient was severely ill and showed little, if any, improvement. Realizing that there was nothing further to offer therapeutically and that she would certainly die if not kept strictly at bed rest, we decided to use prolonged bed rest therapy. After almost one year of this, she began to show definite improvement which has been sustained. It is hoped that the response will be progressive, with eventual return of heart size to normal.

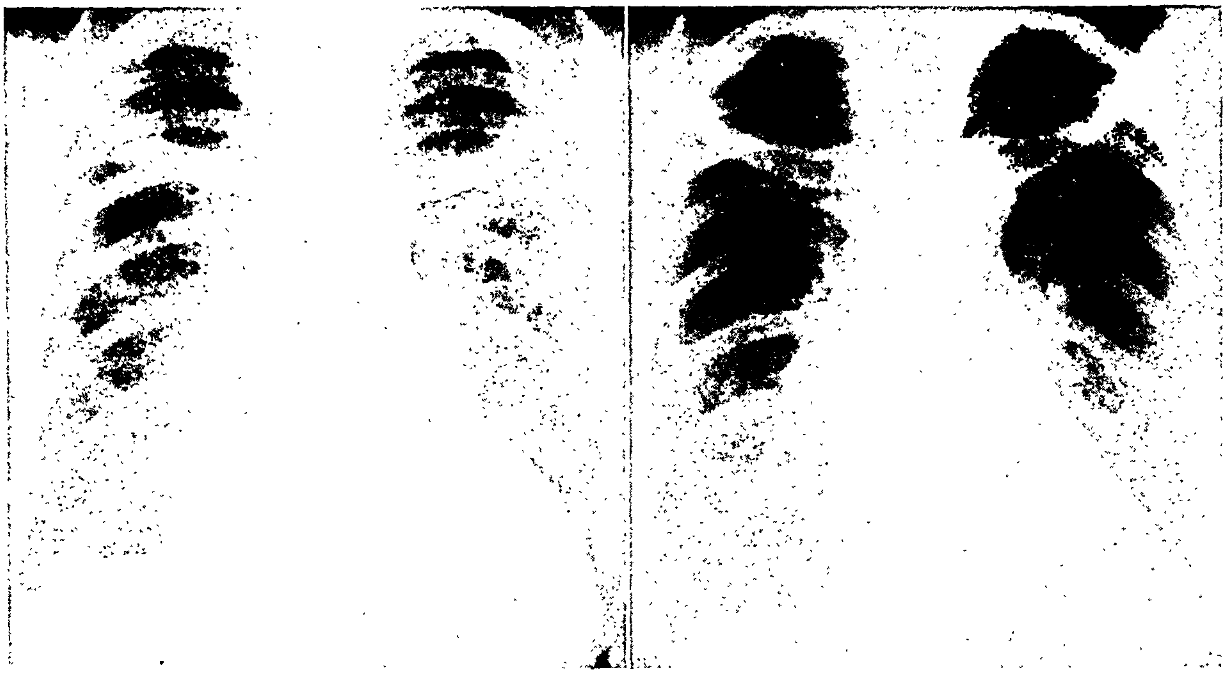

Fig. 3.—Chest roentgenograms of patient taken, *left*, at beginning and, *right*, on completion of 10 months of bed rest.

Comment

Each of these patients has been subjected to extensive diagnostic studies which have failed to reveal the etiological factors responsible for their heart disease. The possibility of the existence of rheumatic myocarditis is a distinct one in case 4, although the only findings consistent with this diagnosis are the patient's age and sporadic prolongation of the P-R interval. On several occasions the latter disappeared after reduction of digitalis dosage. The normal sedimentation rate and lack of any of the clinical or laboratory indications of a rheumatic process are striking. It is our impression, however, that the process from which the patient suffers is nonrheumatic.

Each of the patients had cardiomegaly, a low pulse pressure, and usually an increased sensitivity to digitalis-like preparations. During improvement of the patient, each of these findings disappeared. What most concerned us was that these patients showed marked persistent cardiomegaly in contrast to the acute transitory cardiomegaly of initial heart failure. The latter is a well-recognized phenomenon which rapidly disappears with adequate treatment. These patients showed clinical improvement, but the reduction of cardiomegaly was so slow that, on the basis of previous experience, we expected these patients to show severe cardiac enlargement permanently. The only change in treatment was the addition of prolonged bed rest, to which we ascribed the remarkable improvement observed in these patients.

It is interesting to note that serial electrocardiograms performed on each patient throughout the period of observation revealed definite but limited improvement, with persistence, to a lesser extent, of the alterations commonly ascribed to left ventricular hypertrophy.

The clinical disadvantages of extreme cardiac dilatation are obvious and include embolus formation, rhythm disturbances, and congestive heart failure. Emphasized less frequently, but of at least equal importance, are the mechanical disadvantages of this abnormal state. These are largely due to the alteration of those factors which make the normal-sized heart an eminently satisfactory pump.[2] In essence, the ventricular load, or force exerted on the ventricle, is a product of the blood pressure times the area of the wall which supports the pressure.

In the markedly dilated heart, the minimal decrease in the ventricular size which follows systolic ejection leaves the radius of the ventricular sphere little changed. There is inadequate contraction of internal ventricular surface area in the face of rising pressures so that cardiac work must increase greatly throughout the course of contraction, in contrast to the normal.[3]

By far the major portion of cardiac work arises from the maintenance of myocardial tension. Myocardial oxygen consumption is primarily a function of diastolic size and only secondarily influenced by external work. Control of heart rate and blood pressure by treatment with use of bed rest do much to diminish these burdens. The effects of physical activity include increases in pulse rate, oxygen consumption, cardiac work, output, and stroke volume. Manifestly, patients with cardiac disease of sufficient severity to produce cardiomegaly of the degree discussed can in no fashion be considered "trained" in the usual physiological sense. Accordingly their cardiovascular responses to exertion will be disproportionately large and detrimental.

The cited disadvantages of extreme cardiac dilatation, all present at complete rest, are exaggerated with increasing physical activity. As the patient progresses along the spectrum of decreasing cardiac reserve to the stage of irreversible cardiac dilatation and insufficiency, he reaches a point at which he becomes unresponsive to any and all forms of therapy. It is our contention that the application of long-term bed rest not only delays in time the attainment of the point of no return but may, in selected cases, postpone this catastrophe indefinitely. The latter is a distinct possibility in those young patients whose cardiac size and efficiency can be returned to normal after a single, terminated insult, such as the myocarditis of infectious, allergic, nutritional, or toxic origin.

The therapeutic approach described herein presents many problems quite similar to those encountered in the treatment of pulmonary tuberculosis. An adequate number of hospital beds, cost of long-term hospitalization, and ancillary services would have to be provided, perhaps from resources available but currently unused, in the treatment of tuberculosis. Patient and physician acceptance would have to be won. Even as the administrative problems present themselves, purely medical questions arise to be answered. These are concerned with the time course of response to prolonged bed rest, the identification of those patients who will respond to such therapy, and the significance and permanence of benefits accruing from reduction of heart size to normal.

Summary

Five patients with severe persistent cardiomegaly due to myocardial degeneration of unknown etiology were treated and observed for periods up to one year. The failure of cardiac enlargement to respond to conventional therapy was followed by marked decrease in cardiomegaly when long-term bed rest in a cool comfortable environment was added to the treatment program. So gratifying were the results that this preliminary report was made in spite of the obvious limitations of the study. Further long-

term investigations of this sort are necessary to answer the questions posed by the initial experiences described herein. Nevertheless the serious implications of persistent cardiomegaly warrant such efforts and amply substantiate our contention; however good the objective and subjective response to therapy, no patient with residual cardiac enlargement can be considered cured.

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TOTAL REHABILITATION OF THE LONG-TERM PATIENT

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What is a long-term patient? The National Conference on Care of the Long-Term Patient defined a long-term patient as one who is suffering from chronic disease or impairments and is likely to need, or has received, care for a continuous period of at least 30 days in a general hospital or care for a continuous period of more than 3 months in another institution or at home, such care to include medical supervision and/or assistance in achieving a higher level of self-care and independence. Programs for the total rehabilitation of these patients must be medically directed and supervised and require frequent reassessment and reevaluation for maximum effectiveness. Great strides have been made in the engineering and electronic sciences, including our current accomplishments with satellites toward the exploration of outer space by man. Has the rate of increasing adequate facilities and the training of professional personnel for the care of the sick and disabled kept stride with the ever increasing load? It is generally agreed that it has not, even though the accomplishments in medical care in the last few decades have been phenomenal.

The United States has about 30 million people, out of a total population of 178 million, with varying degrees of chronic disease or impairment Mere prolongation of life is an empty achievement unless the sick and the handicapped are helped to regain the maximum level of self-help to attain a useful, dignified life. About 20 million Americans enter hospitals each year. About 16% of persons with chronic disease are under 35 years of age. Unless adequate maintenance rehabilitation is continued, the danger that a partially disabled person will deteriorate eventually to a state of total dependency is real. The problem of rehabilitating the long-term patient is therefore one of tremendous magnitude. To keep pace with an increasing population, the number of personnel as well as the number of approved facilities must be increased to provide care and rehabilitation. Adequate medical direction is essential.

Statement of Problem

While the immediate goal is to save lives, the long-range objective of total rehabilitation is to return the disabled to useful, productive living with happiness, dignity, and a feeling of being wanted. The lengthening of the human life span from 49 years in 1900 to about 70 years today presents us with about 30 million people, out of a total population of 178 million, with varying degrees of chronic disease or impairment. Between 1900 and

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1950 the population of the United States doubled, while the number of persons aged 65 years and over had quadrupled. As our population continues to increase, and it has been estimated that by the year 2059—one hundred years from now—the population in the United States will be one billion, there will be an inevitable increase in the incidence of chronic illness, both physical and mental, with its associated disabilities.

The problems associated with the total rehabilitation of these persons must be faced with imagination, understanding, and realistic operational plans. Life is being prolonged, but it should also be enriched. The sick must be helped to help themselves and thereby achieve their rightful happiness.

Medicine can be credited with many outstanding accomplishments. The human life span has been increased; infant mortality has been markedly decreased; communicable diseases are being controlled; dramatic developments have occurred in the management of mental disorders; techniques in surgery, anesthesia, radiation, and the use of hypothermia have advanced to an outstanding level; and physical medicine and rehabilitation have taken their rightful position as part of the total management of the sick.

Blood banks, bone banks, eye banks, blood-vessel banks, and skin banks are rapidly assuming stature in medicine. The future may see organ banks, so that other human organs may be transplanted from one person to another. The use of plastic and other materials to replace diseased tissue is increasing. Improved and new, almost miraculous, drugs have been developed. Yet, despite these wonderful advances, many unpleasant facts must be faced. The increased incidence of heart disease, the yearly increase in the number of cancer deaths, the rising number of severe disabilities from accidents, such as paraplegia, quadriplegia, and orthopedic conditions, the alarming rise in the incidence of mental disorders, the steadily rising number of disabilities resulting from degenerative diseases, blindness, and impairment or loss of hearing associated with aging and the aged—all contribute to the large segment of the population that needs prolonged care. We remain hopeful that our knowledge in the field of total rehabilitation, of both preventive and definitive care, will continue to increase to provide answers to these serious problems.

There must be sufficient hospitals, rehabilitation services and centers, nursing and convalescent homes, sheltered workshops, homes for the aged, and adequate numbers of properly trained professional personnel to handle this tremendous patient load. It is not a one-man job and must be squarely faced by all federal, state, and community institutions and agencies whose programs should be actively coordinated and integrated, rather than being merely in physical proximity to each other, to achieve the greatest measure of success.

There are over 10 million persons in the United States who suffer from various forms of rheumatic diseases, such as arthritis, neuritis, bursitis, and myositis. Millions have some type of heart disease. Over 2 million persons have had "strokes," with or without aphasia. Millions of others have neurological disorders such as multiple sclerosis, cerebral palsy, epilepsy, parkinsonism, poliomyelitis, muscular atrophies and dystrophies, various mental diseases, and other conditions. Metabolic disorders such as diabetes, obesity, and thyroid and other glandular diseases afflict many others. Hundreds of thousands are disabled from accidents at home, in industry, and those associated with the various means of transportation. There are nearly 400,000 persons in the United States who are either totally blind or have serious impairment of vision. A survey has revealed that 20 million Americans—one out of every eight—enter a hospital each year.

We must be fully aware of and quickly correct an old and, at times, persistent notion that long-term or chronically ill persons are all in the older age bracket. As a matter of fact, about 16% of persons with chronic disease are under 35 years of age. Total care for all of these must be concerned with their health, housing, employment, recreation, other social activities, and plans for retirement when that period approaches.

General Principles of Rehabilitation

Even though there are almost countless types and degrees of disabilities, there are certain general principles that are applicable in an approach to the complex problems of total rehabilitation. The patient almost always is faced, in varying degree, with psychological, emotional, and social problems associated with his illness or injury. Through the combined skills and efforts of all concerned, including the patient's family, he can be motivated and aided on his road to recovery, which frequently may be long and trying. To develop initiative, motivation, and thereby cooperation, the patient must be helped to accept his illness, his hospitalization, and the total program being offered for his rehabilitation; in addition there must be a sincere desire to get well. There should be no penalties attached to the philosophy of getting well, such as a decrease in financial or other aid, or the necessity of being disabled to a certain degree before becoming eligible for this aid. The ability to feed, dress, bathe and perform self-care activities should be encouraged and commended. Rehabilitation procedures must be medically prescribed and instituted early and intensively, for a sufficient period of time, to secure a realistic goal with a minimal degree of handicap.

The patient's ability to perform the optimal number of self-care and daily-living activities, such as those associated with eating, communication, hygiene, dressing, locomotion, and household functions, is the foundation on which to build a life of usefulness. This training must be permeated with realism, for with some patients many of these activities are beyond the realm of accomplishment. When indicated, proper selection of and training in the use of such devices as splints, braces, crutches, canes, artificial extremities, and wheel chairs must be available. For those who, due to their disability, cannot return to their former type of work, a realistic vocational goal should be established, which may be a full-time or part-time, sheltered work environment or even home-bound work. For the disabled homemaker, the proper placement of kitchen appliances (sink, dishwasher, cleaning utensils, cabinets, and other items) will be most helpful.

Some persons, especially those with chronic illness and specifically those in the older age group, may find a good life in suitable nursing homes, domiciliary centers, and other sheltered situations. Many can live happily at home, with partial or full aid from a homemaker service. It is neither necessary nor beneficial, and certainly not economically sound, to keep patients in general or special hospitals once they have secured maximum hospital benefits; however, there should be continuity of rehabilitation activities when that person is transferred to other institutions or his home.

It is interesting and important to note that there are about 25,000 nursing homes in the United States, with a combined total of nearly 450,000 beds. Ninety per cent of these homes are privately owned and are occupied by persons whose average age is 80 years and less than one-half of whom can walk independently. All relevant agencies and groups must not only be concerned with the problem but must contribute their efforts and funds toward increasing and improving these facilities. These institutions must not supersede or supplant rehabilitation services in hospitals (general, psychiatric, and tuberculosis) or rehabilitation centers but should be equipped for continued maintenance activities. Otherwise there is great danger and risk that partially disabled persons will deteriorate to the stage of eventually being totally dependent. The most vital requirements are adequate medical supervision and accident and fire prevention measures. Hand rails, bath tub and shower grab-bars, nonslippery floors, avoidance of scatter rugs, and other safety measures are indicated. A complete and careful analysis must be made of each person to determine his specific needs and where and how they can be most effectively fulfilled.

Definition and Scope of Physical Medicine and Rehabilitation

Physical medicine and rehabilitation are part of the total management of the sick and include diagnosis of, prescription for, and treatment of disease, defect, or injury by the use of physical measures and the restoration of the patient to his optimal physical, mental, social, and vocational usefulness.

While the medical aspects of the care of the sick should be under the direction and guidance of physicians, medical rehabilitation should be the responsibility of the physiatrist (physician specialist in physical medicine and rehabilitation), who is specially trained to render this type of specialized care. A physical medicine and rehabilitation service usually is staffed by a physiatrist, a rehabilitation coordinator, and various groups of therapists whose activities are integrated with the other services, such as medical, nursing, dietetic, social work, vocational counseling, and others. This group of services again is closely integrated and coordinated with the available government and private agencies and services. All available resources should be explored. The patient's posthospital planning must be initiated early during hospitalization and frequently leads to early discharge and a reduction in the incidence of readmissions. Posthospital follow-up, including reevaluations, by the physician, social worker, public health nurse, and others are important to prolong the rehabilitation benefits and also decrease readmissions, thereby making beds available for others who require hospitalization. A vital factor that is frequently overlooked in planning discharge is the importance of having the patient participate in this planning to the extent of his abilities.

Further, regardless of where the patient is going on discharge from the hospital, but especially if he is to go home, his family should be carefully advised as soon as possible as to their responsibilities in the home management, exactly what care is indicated, and how and where this can be secured. This will surely aid both the patient and his family to better accept and solve any existing problems. The physician has a sacred and great responsibility in directing this over-all planning.

Physical medicine and rehabilitation can be considered as consisting of three phases that overlap to a degree but have continuity, namely, medically prescribed preventive, definitive, and maintenance rehabilitation.

Preventive Rehabilitation.—This phase consists of sufficiently early institution of procedures, even though a patient is unconscious as, for example, after an accident or "stroke." Proper positioning in bed and the use of splints and passive movements of the extremities to prevent contractures and deformities and to aid circulation should be part of the program.

Definitive Rehabilitation.—During this second phase, specifically prescribed rehabilitation procedures are instituted to prevent deconditioning and to enhance function for the performance of the optimal number of self-care activities. It is never necessary to wait until the patient can be taken out of his bed, for treatment can be accomplished at the bedside. When illness strikes, the patient always experiences a measure of anxiety, apprehension, and fear. Entering a hospital or other institution may be a frightening or even horrifying experience for some. An active program, with proper orientation, aids the patient in his psychological and emotional adjustment to his illness and hospitalization.

Maintenance Rehabilitation.—In this third phase of rehabilitation, therapeutic procedures are continued even after the patient's discharge or transfer to another institution, nursing home, or his own home so that he can at least maintain his accomplishments and not regress. In certain progressive disorders the continuation of maintenance activities by the patient is frequently impossible.

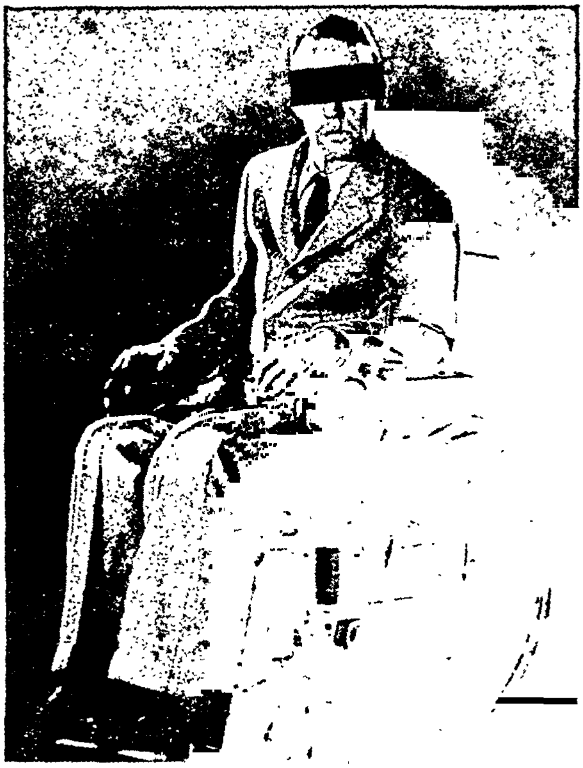

Fig. 1 (case 1).—Patient who sustained high cervical spinal cord injury with resulting quadriparesis. Unable to walk or to propel wheel chair, he operates electric wheel chair. With aid of simple hand assistive devices he performs numerous daily living activities.

To make total rehabilitation available to the sick is not only our moral obligation and responsibility, it is economically sound. The following three case reports illustrate the value of intensive total rehabilitation in severely disabled persons:

Reports of Cases

Case 1.—A young hospital administrator sustained an accidental, high cervical spinal cord injury, which resulted in complete quadriplegia. With intensive application of the procedures of physical medicine and rehabilitation, this patient, who at first could not perform any self-care activities, progressed to the point where, with the aid of simple mechanical devices, he can now accomplish numerous hand activities such as feeding, shaving, brushing teeth, combing hair, writing, painting, stenciling, using a dictaphone, and many others. Realistic ambulation was not practical. Being unable to propel a wheel chair, a great measure of independence and mobility were secured by having him operate an electric wheel chair (fig. 1). His ability gradually to perform these daily-living activities has helped a great deal in enhancing his motivation. Even though his disability remains, it constitutes only a minimal handicap in his job performance, for he will return to his former type of work as an administrator. His mental ability is not impaired, and he presents no vocational problem. This patient well demonstrates the importance of the use of mechanical devices to aid in the performance of daily-living activities, which would otherwise be impossible.

Case 2.—Subsequent to an accident, a 42-year-old mechanic was subjected to a traumatic, high amputation of both lower extremities 2 in. below the perineum. Due to contractures, these extremely short stumps were in an abducted position, with limited movement. He was fitted with short bilateral pylons (temporary artificial legs) which re-

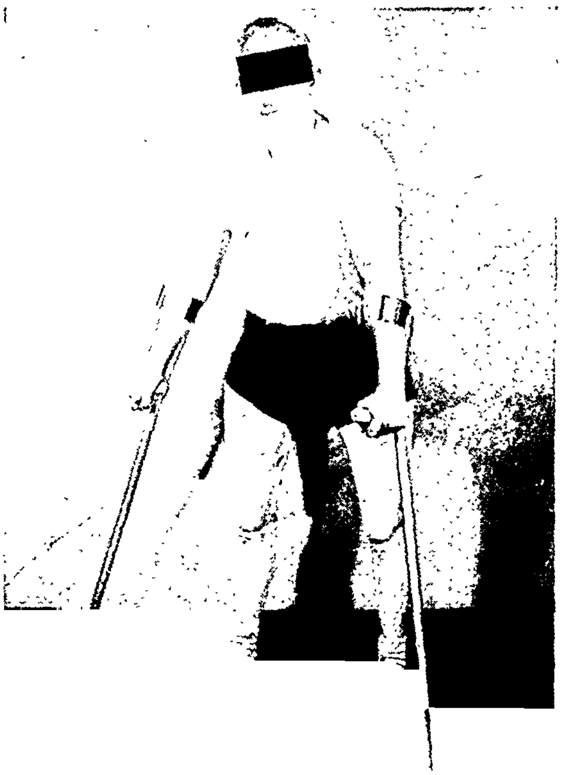

Fig. 2 (case 2).—Patient who underwent bilateral, extremely high, traumatic amputation of legs walks with permanent artificial legs and forearm metal crutches. He safely drives hand-controlled automobile, ascends and descends stairs and curbs, performs all self-care activities, and is gainfully employed.

duced his normal preamputation height by 12 in. to facilitate his learning to balance and walk in the parallel bars. He then learned to walk, first with use of long crutches and then with short, metal forearm crutches. When this stage had been mastered, the pylons were lengthened to raise him to his normal height. He again resumed his ambulation training, which included ascending and descending stairs, stepping on and off curbs, getting in and out of various types of chairs, driving a hand-controlled automobile, and other activities. He finally learned to walk really well with permanent artificial legs and forearm metal crutches, as shown in figure 2. During his rehabilitation, he was given intensive general conditioning exercises to maintain good body tone and maximum muscle strength of the remaining muscles, primarily those of the trunk and upper extremities. He is living at home, has returned to a bench type of mechanical work which he performs in a commendable manner, and is completely independent. He drives a hand-controlled automobile to and from his job, and, even though his disability is an extremely high bilateral lower extremity amputation, the resultant handicap with regard to his job and daily-living activity performance is minimal.

Case 3.—This 39-year-old machinist developed a severe case of Parkinson's syndrome, with marked rigidity and tremor, after an attack of encephalitis. When he was admitted to the Veterans Administration Research Hospital of Chicago, his disability, for nearly three years, had been quadriparesis, with flexion contractures and deformities of both hands and wrists and both lower extremities, with the feet in an equinus position. He was unable to perform any daily-living activities and was more or less confined to bed. After receiving intensive physical medicine and rehabilitation procedures, this patient was able to learn to walk with the use of a pick-up walker, thereby eliminating the need for a wheel chair. Weighted metal runners were attached to the walker to secure greater stability and decrease in tremor while walking (fig. 3). This patient is unable to walk safely with crutches but walks safely about his home and on the street with the walker. Drop foot braces on each leg are necessary to hold the foot in a supported position. On discharge to his home, this man was able, in slow fashion, to feed himself, brush his teeth, comb his hair, and perform other hand activities with the aid of simple, plastic devices. He can now dress with some assistance and climb stairs with use of a handrail, but his speech remains slurred and indistinct, in spite of speech therapy. He enjoys a good measure of independent living.

In addition to the many therapeutic procedures rendered by the physical medicine and rehabilitation service, numerous diagnostic measures are available.

Vocational Counseling and Selective Job Placement

Manpower and human dignity are our greatest resources and must be developed and conserved. Return to gainful employment is frequently not the only vocational goal, for many persons, because of their age, their disability, and their general socioeconomic circumstances, cannot and will not attain this goal. However, many can enjoy independent living with restored dignity through the ability to perform daily-living activities by themselves, or with minimal assistance, and perhaps with homemaker service help. The number in this latter group will, in all probability, parallel the number of those who are over 65 years of age. In 1900 about 4% of the population in the United States was aged over 65, while in 1958 the percentage rose to about 12%, and it has been predicted that by the year 2000 16% of the population, or about 30 million persons, will be over 65 years of age.

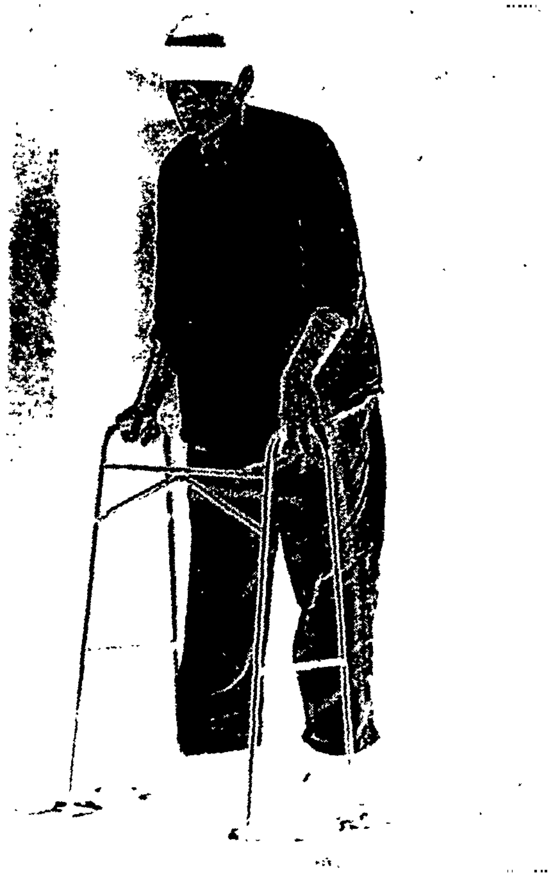

Fig. 3 (case 3).—Patient with postencephalitic Parkinson's syndrome resulting in quadriparesis with rigidity and tremor. He walks with pick-up walker equipped with weighted runners for added stability and lessened tremor. He wears bilateral drop foot braces to correct equinus position of feet. Note deformities of hands, especially left.

The old and revolting concept of retirement according to chronological age must be supplemented by a more just view based on the individual person's ability to perform various tasks in business and industry. The productive capacity of persons over 65 years of age is a tremendous and potent factor in our nation's economy and social structure. There is a highly rated law school in the United States whose entire full-time faculty is over 65 years of age.

The success of any rehabilitation program that endeavors to return the maximum number of persons to productive living will depend a great deal on selective job placement. The over-all medical picture is the keystone to any exploratory work objectives in which the individual person's physical and mental abilities to perform are carefully matched to the physical and mental requirements of the job under consideration. In this manner, even though a disability exists, the handicap to performing a specific job is minimized and in many instances does not exist. The words "disability" and "handicap" must not be confused or used interchangeably. Work in which the disabled person is properly placed has a beneficial effect on his mind and body as well as on his family's morale and outlook.

Research and Future

Greater amounts of hard work, dedication, and available working funds are needed to allay or, perhaps, conquer the afflictions of mankind. Research, both basic and clinical, hand in hand with the highest caliber of medical care brings hope.

It is possible to predict things to come which will make life longer and, at the same time, more beautiful and rewarding. Death from infectious and communicable diseases will be rare. The mortality from cardiovascular diseases will decline. The death rate from cancer will drop as spectacularly as that associated with pulmonary tuberculosis and tuberculous meningitis after the discovery of streptomycin, isoniazid, and other drugs. Prevention and improved therapy in all of the rheumatic diseases is probably just beyond the horizon. Poliomyelitis soon will be just as rare as the dreaded diphtheria of yesteryear. The "common cold" will be controlled and probably conquered. The rate of the degenerative processes associated with aging will be markedly decreased so that man's years will extend beyond the biblical threescore and ten.

Summary

The problem of the rehabilitation and care of the long-term patient is of tremendous magnitude. Both the increase in population and the increase in the human life span bring us face to face with the realization that the number of persons with illness and injury will parallel these increases. Procrastination should not enter into our deliberations regarding their proper management, which should be as follows.

Medically directed rehabilitation services must be established in all hospitals (general, psychiatric, and tuberculosis) to initiate indicated activities promptly. The number of approved rehabilitation centers, nursing homes, homes for the aged, and other suitable living environments, all under medical supervision, must be increased throughout the country. Means for the continuity of rehabilitation must be established, so that transfer to these institutions will not produce a gap in maintenance activities of the patient.

The number of trained professional personnel to handle the growing numbers and needs of the sick and disabled must be augmented by increasing school facilities and educating prospective students to the opportunities in the field of improving the health of our nation.

All care programs should be developed and centered around the patient's individual requirements. "Production" or "conveyor belt" programs will never be successful.

Success in total care depends to a great extent on the initiation of an adequate, intensive rehabilitation program for a sufficient period of time. Jointly integrated planning, both hospital and posthospital, by all professional persons dedicated to the over-all care of the sick not only will bring maximum results for the patient but will make for increased patient bed turnover and decreased hospital and institutional readmissions. Realism must permeate all our thinking and planning, for not all patients will walk again, nor will all persons be employable.

There always should exist the willingness to exchange ideas among all professional people to enable everyone to benefit from the experiences of other persons and agencies. This concept is vital for successful patient care.

In the minds of not only professional people but the public, through education, must be inculcated an awareness and understanding of the problems and needs of the sick and how these can be relieved to make their lives purposeful and fruitful. The philosophy of rehabilitation must permeate all people engaged in the care of the disabled.

Continued education of the patient, his family, his friends, and his employer as to the hopes and realistic goals of the disabled, coupled with continued, increasing basic and clinical research and the untiring efforts of dedicated people will bring gratifying results and a greatly improved outlook. We must move forward, for today's seemingly insurmountable complexities of certain illnesses and injuries will be tomorrow's conquering achievements. Along the way, in the tradition of our noble profession, we will reap the rich, personal reward of our patients' gratitude.

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The medical illustration service and the manual arts therapy section of the physical medicine and rehabilitation service at the Veterans Administration Research Hospital supplied the photographs used in this article.

ORIGINS OF AMERICAN SURGERY

Edward D. Churchill, M.D., Boston

The year 1850 is a convenient marker to indicate the beginnings of surgery as it is known today. The midcentury point is chosen not merely as a convention but because it best indicates the approximate time of the first impact of science on the ancient practical art of surgery. This essay will consider surgery as a component—an activity—of medicine as a whole, and medicine as an expression of the culture of western society. Then, the progress of surgery can be plotted against the development of the scientific attitude, showing a progressive change that has been the predominate force in thought and action since the great scientific revolution.

A brief glance at the more remote background of surgery discloses many trends and events that began to be felt within surgery only after the midpoint of the 19th century. The most powerful of these forces was the scientific revolution which reached its completion about the year 1800. Hall[1] has given the limiting dates for the scientific revolution as 1500 to 1800 and concludes his study with the statement that "Much more has been learnt about Nature, from the structure of matter, to the physiology of man, in the last century and half than in all preceding time."

Emergence of Surgery

During the 18th century, in which the surgery of France was supreme, came the liberation of surgery from the yoke of the physicians. Louis XV issued an edict calling for the reorganization of the College of Saint-Côme and the creation of chairs for surgeons to demonstrate the principles of anatomy, the treatment of surgical disorders, and operations on cadavers. The edict of 1724 provoked violent protestations from the faculty of medicine, and its members marched in full academic regalia to the college, only to find the doors to the amphitheater closed firmly against them.

In the light of the prestige the surgeon enjoys today it is difficult to envisage the centuries during which the surgeon was held in low esteem, not only in academic circles but socially and intellectually as well. The common interpretation is that the surgeon was firmly suppressed by the energetic and corporate interests of the physician. There is more than a grain of truth in this viewpoint. On the other hand, the surgeon who emerged from the Middle Ages was without question an unruly and arrogant ruffian. His stock-in-trade was a modicum of skill, achieved through random personal experience and mixed with much misinformation derived from illogical inferences and assumptions regarding this experience. Development of the scientific attitude by both physicians and surgeons has now joined their interests by the establishment of many points of contact between fields which previously were separated by sharply defined boundaries. Hostility to the "invasion" of these domains from one side or the other has all but disappeared today, and in its place one sees the formation of a united front and a frontier which calls for joint exploration.

It is this same force—the development of the scientific attitude—that can eventually reunite the fragments into which contemporary surgery has been split by the elaboration of technical skills. These expert skills have been developed on the basis of topographical anatomy and pathology. They will be preserved but will be complemented by a broader understanding of structure and function, which inevitably will bring a regrouping in its wake. Today hostility to an invasion into a specialty all too frequently takes the form of a jurisdictional dispute based on posturing designed to defend the interests of a guild.

The old cleavage between medicine and surgery was more disastrous to medicine than to surgery. At the end of the 18th century surgery actually was well in advance of the medicine of that period, which had remained doctrinaire and had become the dream world of the systematists. Morgagni's contribution, therefore, was better understood by surgeons who were accustomed to think in terms of structure and organs rather than in the fantasies of humoral doctrines.

In even the briefest sketch of the background of surgery leading up to 1850, it is necessary to mention names of Vesalius, Paré, and John Hunter. Paré's contributions were notable because they swept away the cobwebs of authority by straightforward observations and by change of method on a trial and error basis. The abandonment of hemostasis by cautery in favor of the ligature was of this order. The decision to discard the use of boiling oil, which was supposed to counteract the venomous nature of gunshot wounds, was made immediately when Paré observed that the results of surgery were better when boiling oil was not used. There was no trace of what can be identified as the scientific attitude in Ambroise Paré. He was a shrewd observer with a tremendous experience, which he recorded in painstaking detail. The fact that he recorded in his voluminous writings the results of his revolts against authority justifies the high position he holds in the history of surgery.

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Read before the Section on Surgery, General and Abdominal, at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

Vesalius and John Hunter occupy a somewhat different position. They were both surgeons, it is true, but their contributions are preeminent because they affected the development of science as a whole rather than because of a direct effect on surgery as a circumscribed field. The great textbook of Vesalius set the pattern for anatomy as descriptive science and far transcended the needs of operating surgeons for centuries to come. It is the Vesalius who worked as an anatomist, not Vesalius in his role as a surgeon, of whom surgeons may be proud. Somewhat the same can be said of John Hunter, memorialized as the founder of scientific surgery. While Hunter made more direct contributions to the surgery of his time than did Vesalius, nevertheless it is John Hunter the biologist, working to correlate structure with function, who is important in the history of science as a whole.

Philip Syng Physick

Let us pick up the thread of American surgery around the date of 1800, which, as has been said, marks the completion of the scientific revolution and closely coincides with the beginning of the United States of America as a new nation. The life of Philip Syng Physick spanned the close of the 18th and the beginning of the 19th century, for he was born in 1768 and died in 1837. He also was probably the best educated surgeon of his generation. Physick had the good fortune to be a student of John Hunter, for when he was 21 years of age, in the year 1789, his father took him from Philadelphia to London to finish his medical education. He became more than a pupil of Hunter; it is said that a great intimacy grew up between the "rough and tough old Scotsman and the precise, methodical, prim, Philadelphian." The meticulous dissecting skill of Physick was greatly admired by the master. Physick was taken into the family, and ultimately Hunter wanted him for a partner. With Hunter's sponsorship Physick was made house surgeon at St. George's Hospital. If he had chosen to stay in London, Physick would have taken a place with other famous pupils of John Hunter—with Astley Cooper, Abernethy, Home, John Thompson, and others, but he went to Edinburgh to complete his studies and in 1792 returned to Philadelphia. The active professional life of Physick was to last through 45 years. When he died "he was eulogized throughout the land; from Boston to Louisville," and became known as the "Father of American Surgery."

In 1903 James Gregory Mumford, a surgeon himself but a semi-invalid for many years with advanced mitral stenosis, wrote a brief sketch[2] of Philip Syng Physick after a careful study of the biographical material then available. (It is of interest that the tight mitral valve in Mumford's heart led Cushing to encourage Cutler in early attempts to relieve mitral stenosis by surgical methods.) The date of Mumford's writing, 1903, is significant, for at that time Mumford found the Philadelphia career of Physick a complete enigma. His curiosity was aroused by the inconsistencies apparent in Physick's career, but, writing against the 1903 background, he was unable to put his finger on the key. "He should have put his enormous experience and surgical knowledge in print," Mumford wrote. "For the lack of such a book he has become a myth for us." Taking the life of Physick for a text, the only moral Mumford could find lay in the "unwisdom of an existence with but one idea. A salient thing with him was practice. He knew nothing else." Although his practice was a large one and although it is noted that John Marshall, the great chief justice, was numbered among his patients (it is said that 1,000 stones were removed from his bladder by lithotomy) and although he achieved a reputation as a brilliant hospital operator and clinician, the fame of Physick seemed almost out of proportion to his deeds. Yet Mumford dwells on the fact that Physick's contemporaries felt in him the great man. There must have been something, Mumford admits, which has not come down to us.

Only after exhaustive research might one venture to add an interpretation of Philip Syng Physick to the contributions that have been written about him. From a vantage point in the middle of the 20th century, however, it is possible that Physick's career might be more understandable than it was to Mumford at the turn of the century. John Hunter the biologist and his pupil Philip Syng Physick are closer to American surgical thought today than they have been at any intervening period. The American surgeons of 1800 were not ready to hear the teachings of John Hunter, far less to accept them. As a hypothesis it may be suggested that on his return to Philadelphia Physick became a disillusioned man reluctant to write in the dogmatic style of the times, standing aloof from his contemporaries, and seeking but not finding satisfaction in his brilliant technical feats. He was frustrated by his failure to find a receptive listener with whom he might share the insights he had received from his great biologist and surgeon teacher, John Hunter. It may not be mere coincidence that he suffered from chronic dyspepsia.

In 1818 Physick gave up the chair of surgery for the professorship of anatomy, but the descriptive anatomy of that period was dull and dreary and the medical students of the day were an uneducated and uninspiring lot. He died as a lonely old man, and possibly his last act can be interpreted as a final gesture of contempt for the learning of the time; he left orders that no postmortem examination of his body should be made and that he should be buried in a double coffin with a guard maintained over his grave for six weeks after burial.

Physick lived in a period in which the surgery of the new world was building its foundation from the surgery of the old world. This process was to go on for many decades, but one sees little trace of the scientific attitude of John Hunter until the 20th century. The story of early 19th century American surgery is largely the saga of Paul Bunyan exploits by stalwart bearded pioneers. The error which nullified their endeavor was the fixed belief that perfection in surgery resided in the knowledge of anatomy and the rapid execution of the operation. The fundamental problem was that of postoperative incisional infection. The expert anatomists and rapid operators did not perceive that their most brilliant efforts came to naught because they carried with them on their hands, on their instruments, and on their dressings, the germs of contagion which led to infection and oftentimes to death. The surgery of 1850 was in many respects inferior in results to that of the century before; crowded hospitals, increasing numbers of autopsies, and operations on cadavers added to the contagion, and surgery of the simplest kind became a disheartening and frustrating undertaking.

French surgery held supremacy during the 18th century. It is of interest that the beginning of the development of the scientific attitude in internal medicine appeared in Paris in the first decades of the 19th century. The new attitude was limited to the physicians and was transmitted to America by young physicians who studied there to complete their education. Parisian surgery, at this time of influx of students from America, presented a forbidding picture to a young man. It was dominated by Dupuytren (1777-1835) who was both violent and despotic and known as "le brigand de l'Hôtel-Dieu."[3] Despite his personal unattractiveness, Dupuytren was a great pathologist and clinician who, with Laënnec, had picked up the anatomic-clinical concepts of Morgagni. The scientific stirrings in Paris in the opening decades of the 19th century may have had some indirect influence on American surgery through the physician colleagues who worked with Louis and other notable clinicians of that period, but the influence was scarcely perceptible.

The Revolution in Biological Science

Hall, whose date of 1800 I have accepted as marking the end of the scientific revolution, designates the period 1830-1870 as the subsequent period of "biological revolution" which completed the modern scientific outlook. This movement brought the natural sciences into biology, and it was as a part of the biological revolution that surgery started to move forward. The accomplishments in medicine in Paris coincided with the first phase of the biological revolution and consisted largely in bringing precise measurements and observations to the bedside of patients. Louis, in particular, introduced numerical thinking into medicine. The impact of the biological revolution on surgery was further delayed, for it had to await a more tranquil atmosphere in the operating theater. This was achieved through the advent of general anesthesia, which did away with the barbaric conditions under which operations were performed.

The significance of the universal acceptance of general anesthesia by sulphuric ether and shortly thereafter by chloroform must not be measured solely by humanitarian considerations for the patient and the tranquility it brought to the operating room. Both agents, and also nitrous oxide, were *materia chemica*—compounds produced by the chemist. The ancient art of alchemy had suddenly come into its own and produced compounds that quickly attained a major place in the therapy that was so dear to the heart of the practitioner. Surgery was not yet freed from the bonds of infection, but a new era was beginning for all of medicine—an era in which the healing art was to be armed and guided by science. It is for this reason that I have chosen the date of 1850 as the beginning of surgery as we know it today. By 1850 surgery was ready to expand its base from anatomy and morbid anatomy to the newly forming biological sciences.

The event destined to liberate surgery completely came in less than two decades and was, of course, the application of Pasteur's concept to the age-old problem of incisional infection. The contribution of Joseph Lister in 1867 removed the final barrier to surgical endeavor.

By 1855 American students seeking to complete their medical education abroad turned toward the German-speaking countries of Europe. They went beyond Edinburgh and London, where their grandfathers had studied with Syme and Astley Cooper; they went beyond Paris with its crowded hospitals where their fathers had walked the wards with Louis and learned to use the stethoscope of Laënnec; they went to Vienna and Berlin and to other university centers of Germany and Austria. Here they absorbed the teachings of Carl Ludwig, Rudolph Virchow, and other apostles of the new order in the science of medicine.

Surgical technology developed for a time largely under its own momentum. Acceptance of Lister's principles became universal during the 1890's. The exploitation of the concept of asepsis in the development of surgical technology was projected well into the 20th century and, in fact, goes on today. There is a temptation to accuse the surgical technologists of the closing decade of the 19th century and of the early decades of the 20th century of having neglected the general condition of their patients, in an intense preoccupation with operative techniques. It must be remembered, however, that surgical technology burst on the world and developed rapidly before systematized knowledge became available for the interpretation of the many complex mechanisms and reactions that attend surgical disease and, indeed, the operation itself. Until the vague and ill-defined clinical symptoms of disease could be translated into rational biological, chemical, and physical terms, their control and management were of necessity undertaken on an experiential basis or ignored altogether. The operation as a technical undertaking forged ahead of the knowledge required to guide and control its use. For this reason the operation appeared as, and actually was, a dangerous affair, despite asepsis, and it not infrequently ended in disaster. But with all its hazards the operation was frequently the only measure that could offer any semblance of rational treatment under exigent circumstances.[4]

The date of 1870 has been offered as marking the close of the revolution in the biological sciences. Warren[5] completed his education in Europe in 1869. It is recorded in his reminiscences that the teachings of the old medical world, of which he was a fairly up-to-date product, were even then of the past and that it was time to cast off much that was old and prepare himself for the dawn of a science which was to revolutionize medicine and surgery.

Twentieth Century American Surgery

This prediction has indeed proved true, and there is little need to dwell on the events which merge into the present scene. Surgery, as is characteristic of a useful art, moved slowly in accepting change. Changes in the matured craft of surgery were paced by its gerontocracy, the members of which were a generation removed from the new knowledge emerging from the biological sciences. Ultimately the traditional manner by which the practical art was passed down from dominant master to docile apprentice underwent conversion to an interchange of knowledge between teacher and pupil.

The renaissance of the biological school of John Hunter became visible in American surgery by the early years of the 20th century. It has been gathering momentum steadily. Now, a decade beyond the midcentury mark, American surgeons can be judged worthy to receive the teachings of Hunter's friend and pupil, Philip Syng Physick, the father of American surgery, whom he educated and sent back to us over a century and a half ago.

The rise of the new American surgery based on the biological sciences has met with criticism and opposition from many quarters. Warren answered these criticisms over thirty years ago:

> The appealing aspect of this new trend is the kindly concern for the patient and the feeling engendered that he has finally come into his own. Each patient becomes a special problem worthy of the time and thoughtful consideration of the brightest intellects. The human frame, with its wonderful mechanism and its complex vital processes, comes to be regarded as an intricate machine, each component of which must be taken into account in reaching a diagnosis or seeking a remedy. The operator comes to realize that surgical interference must be accompanied by eternal vigilance as the price of success. It does not seem to be too extravagant an expectation that this new biological surgery is destined to open up another era full of aid and comfort to suffering humanity.

32 Fruit St. (14).

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GENETICS AND CONSANGUINITY.—The basic genetic effect of consanguineous matings is to increase the number of individuals carrying the double dose of recessive gene. Assume that a healthy subject carries a single dose (heterozygote) of a rare gene a, which in double dose (aa) produces clinical manifestations. Only a marriage with a person also carrying gene a would be of importance since one-quarter of the offspring of such a mating could inherit both abnormal genes (aa). First cousins share common grandparents; they are therefore much more likely to carry identical genes derived from a common ancestor than are unrelated individuals. Recessive diseases will thus be much more common among the children of cousin matings. . . . Since consanguinity effects may be of great help in the identification of difficult diagnostic problems, such as recessive diseases, it is desirable to note this criterion in obtaining family histories. In eliciting a possible history of cousin marriage, it is helpful to note the patient's name, the mother's maiden name as well as both the paternal and maternal grandmother's maiden names. If any two of the possible four names are identical, it is not unlikely that a cousin marriage exists.—A. G. Motulsky, M.D., and S. M. Gartler, Ph.D., Consanguinity and Marriage, *The Practitioner,* August, 1959.

DANGERS OF PROLONGED ANTICOAGULANT THERAPY IN HEPATIC DISEASE

DIATHESIS AND INTERCURRENT ACUTE HEPATITIS

William F. Kliesch, M.D., Philip C. Young, M.D.
and
William D. Davis Jr., M.D., New Orleans

After a myocardial infarction a man took 50 mg. of phenindione twice daily as anticoagulant prophylaxis against possible recurrences. After four years of this therapy, at age 54, he was admitted to the hospital with nausea, vomiting, jaundice, and various hemorrhagic manifestations. The findings here reported indicated that intercurrent acute hepatitis potentiated the effects of the anticoagulant. It is recommended that patients receiving prolonged anticoagulant therapy be watched for the appearance of conditions, such as hepatic and renal disease, diabetes, and blood dyscrasias, in which the use of anticoagulants is known to be temporarily or permanently contraindicated. The patient recovered from the hepatitis, and discontinuation of the anticoagulant therapy was not followed by any progression of his heart disease.

Prolonged anticoagulant therapy after myocardial infarction or other vascular accidents is a well-recognized, although much-debated, medical practice,[1] since it entails significant risks. Advocates of prolonged anticoagulant therapy recommend that, among other things, the patient be intelligent and cooperative and that frequent prothrombin determinations be obtained.[2] The usual contraindications to anticoagulant therapy include renal disease with elevation of the blood urea nitrogen level, hepatic disease, shock, purpura, age of more than 70 years, diabetes, severe congestive heart failure, blood dyscrasias, recent neurosurgical operations, peptic ulcer, catheter or Wangensteen suction, hemothorax, positive reaction to fecal examination for occult blood, and persistent hemoptysis.[3] Difficulties may be occasioned by failure of the patient to report for frequent examinations and prothrombin determinations or by occurrence of intermittent complications. The following case is an example of the latter. Severe hemorrhagic diathesis developed secondary to acute infectious hepatitis while the patient was receiving phenindione. As far as we have been able to determine, this complication has not been previously reported.

Report of a Case

A man, aged 54 years, was admitted to Ochsner Foundation Hospital on April 14, 1958, because of jaundice of one day's duration. Two weeks before admission he had complained of nausea, vomiting, and general malaise. For one week his stools had been light-colored, and he had noted bleeding on blowing his nose and streaks of blood in his sputum. On occasion bright red blood had been found in his stools. The patient had been taking 50 mg. of phenindione twice daily for the last four years, since a myocardial infarction. The last determination of prothrombin time had been obtained seven weeks before admission, when he had had a complete examination including blood tests, roentgenography of the gastrointestinal tract, electrocardiography, and basal metabolism test. During the four years he had been taking anticoagulant therapy he had seldom consulted the same physician twice, since his occupation required that he move from town to town. The prothrombin time had been determined every six weeks to two months, depending on the availability of laboratory facilities. It had never been found to be excessively prolonged, although on several occasions the patient recalled having excreted dark urine.

Approximately one year before admission iron deficiency anemia was diagnosed. The patient denied exposure to toxic solvents. He admitted excessive indulgence in alcohol, with inadequate food intake, between the ages of 27 and 39 years. Two siblings (both with a long history of alcoholism) had died from pneumonia.

On admission the patient was deeply jaundiced. The vital signs were normal. Numerous petechiae were noted over the entire body and a large ecchymotic area measuring 10 by 12 in. covered the right side of the chest. The liver and spleen were not palpable. Diffuse tenderness was detected in the right lower abdominal quadrant, and intestinal sounds were normal.

On admission the hemoglobin level was 11.3 Gm. per 100 ml., the hematocrit 36.5%, and the white blood cell count 6,500 per cubic millimeter, with 70% polymorphonuclear neutrophils, 1% basophils, 3% eosinophils, 22% lymphocytes, and 4% monocytes. The urine was cloudy and red and contained 4+ albumin. Severe hematuria was evident on

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From the Section on Gastroenterology, Ochsner Clinic.

microscopic examination of the urine. On roentgenography of the chest mild cardiomegaly but normal pulmonary fields were noted. Changes consistent with a diagnosis of old posterior infarction were noted in the electrocardiogram. It was the impression of the admitting physicians that the patient was suffering from viral hepatitis, complicated by hypoprothrombinemia secondary to prolonged anticoagulant therapy.

Laboratory Data on Patient Treated with Menadione for Adverse Effects of Prolonged Anticoagulant Therapy

Tests	Week 1st	2nd	3rd	4th	5th	14th
phosphatase (normal, 2-4 Bodansky units)	6.3		7.3			3.1
Total protein level (normal, 6-8 Gm.%)	5.2		6.7			5.7
Albumin level (normal, 3.6-5.4 Gm.%)	3.5		3.6			3.9
Globulin level (normal, 1.5-3.4 Gm.%)	1.7		2.9			1.8
Bilirubin level,						
Direct	20.1	16.9	7.6	2.63	1.80	0.25
Total	32.0	27.7	15.1	5.33	3.80	1.01
Cephalin flocculation						
24 hr	2+					
48 hr.	3+					
Thymol turbidity (normal, 0.7)	13					
Prothrombin time (sec.)						
Control		12.2	11.0		12.0	11.3
Patient		13.4	12.5		12.2	11.9
Serum glutamic pyruvic transaminase activity	1,715		1,747			41
Serum glutamic oxalacetic transaminase activity	4,800		3,900			165
BSP retention, % 45 min.		50		6	5	2

Twenty hours after admission shock developed, at which time the hematocrit was 30% and the prothrombin time prolonged to 335 seconds (control 11.6 seconds). The blood pressure was 90 mm. Hg systolic and 60 mm. Hg diastolic. The shock responded favorably to the usual measures. Twelve hours after intravenous administration of 72 mg. of menadione the prothrombin time decreased to 18.8 seconds (control of 11.7 seconds); five days later it had dropped to 13.9 (control of 13) seconds. Results of other laboratory and hepatic function tests are shown in the table. The patient continued to improve, with subsidence of the ecchymosis and jaundice. On needle biopsy of the liver 20 days after admission, changes compatible with a diagnosis of viral hepatitis in the regenerative stage were noted (fig. 1). On biopsy 23 days later, these acute changes had subsided, and the specimen was interpreted to be compatible with a diagnosis of early cirrhosis of the liver. Small pseudolobules with chronic inflammatory cells, proliferating bile ducts, and swollen granular hepatic parenchymal cells were noted (fig. 2).

By May 31, 1958, sulfobromophthalein (Bromsulphalein) excretion had decreased to 3% at the end of 45 minutes, and the prothrombin time, urine, and peripheral blood picture were normal. The total serum bilirubin level had decreased to 3.28 mg. per 100 ml. The serum glutamic oxalacetic transaminase level was 165 mM. per 100 ml. and the serum glutamic pyruvic transaminase level 45 mM. per 100 ml.

The patient was discharged with instructions to take 5 mg. of prednisone twice daily, one Theragran (therapeutic vitamins) capsule daily, and one-half ounce of brewer's yeast three times daily. His condition gradually improved.

On July 13, 1958, the patient was readmitted for evaluation. Anginal symptoms had occurred on one occasion but they had been transient, subsiding spontaneously and without incident. No significant abnormalities were detected on performance of laboratory studies or physical examination at this admission. The liver, palpated 2 cm. below the right costal margin, was firm, smooth, and nontender, and the spleen was not felt. Continued presence of pseudolobules with fine surrounding fibrotic strands was noted on liver biopsy. Inflammatory reaction in the liver was much less prominent (fig. 3). The cardiologist noted no progression of the heart disease since cessation of therapy with anticoagulants.

Comment

That this patient's intercurrent illness was acute viral hepatitis is suggested by the elevated cephalin flocculation, thymol turbidity, and serum transaminase values, and the reduction in serum protein levels. The first needle biopsy of the liver, performed 20 days after admission, revealed a typical picture of the regenerating stage of hepatitis.

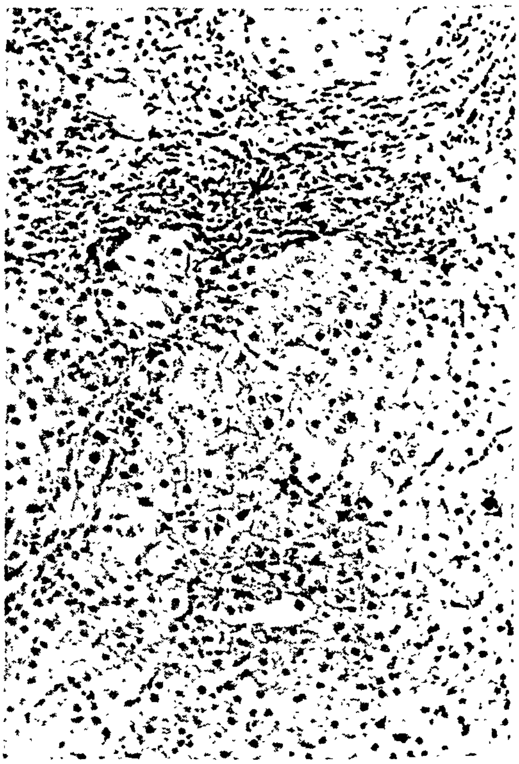

Fig. 1.—Liver biopsy section, 5/3/58: inflammatory response in portal and intralobular situations together with necrosis and stromal collapse.

Whether this represented the changes due to infectious hepatitis or homologous serum jaundice is impossible to state. Six to 12 weeks before admission the patient had received hypodermic medication. It is believed that the hepatitis was not due to a drug sensitivity, as reported by Makous and Van der Veer[4] or East and Beamish.[5] This patient had been taking phenindione for four years and had had no symptoms suggestive of sensitivity to this drug. The acute presenting problem was the hemorrhagic tendency manifested by bleeding into the skin, intestines, urinary tract, and probably the mesentery. Fortunately, this condition responded well to intravenous administration of vitamin K, and apparently no permanent ill-effect resulted.

Hemorrhagic difficulties after anticoagulant therapy have been reported to occur in fewer than 3% of patients presenting uncomplicated cases[1] who are carefully observed, and 10%[4] of those patients who have complicating illnesses. Bleeding occurs most frequently in persons who are older than 70 years of age or who have renal, hepatic, or hematological complications or a local condition that favors bleeding, such as peptic ulceration, indwelling catheter, or gastric suction. Nonetheless, Sise and associates[3b] cautiously prescribed anticoagulants for patients with hepatic disease when they were indicated and noted bleeding complications in 10%. We[6] treated a patient with Chiari's syndrome with bishydroxycoumarin (Dicumarol), without mishap.

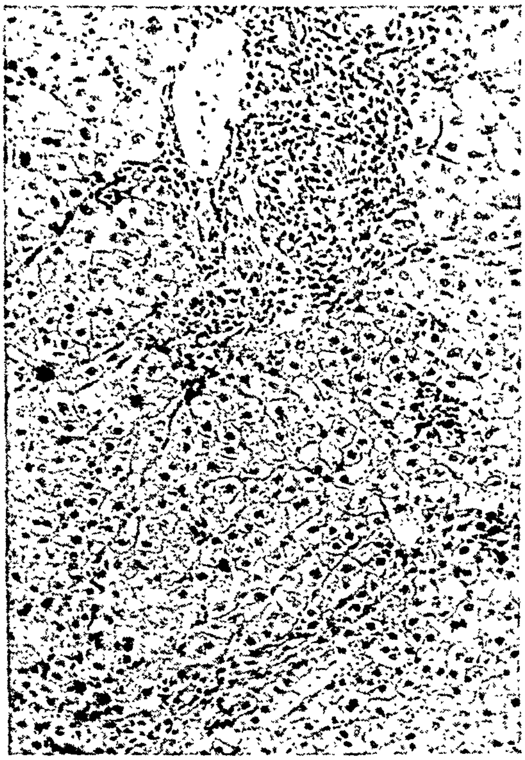

Fig. 2.—Liver biopsy section, 5/26/58: regeneration and bile duct increase with continued inflammation.

In the case herein reported the tendency to bleed represented potentiation of the effect of the anticoagulant by intercurrent hepatitis. The anticoagulant properties of phenindione and similar drugs depend on their ability to inhibit prothrombin formation. Other factors, such as proconvertin and plasma-thromboplastin, are also inhibited.[7] Acute hepatitis, with its widespread hepatocellular damage, interferes with the normal production of prothrombin.[8] There are no significant stores of prothrombin in the body, and the prothrombin concentration falls rapidly, paralleling the degree of hepatic damage.[9] In hepatitis alone the prothrombin time may be greatly prolonged, and its level appears to be conditioned by the severity of the illness.[10] Others[2a] have noted an exaggerated response to anticoagulants in patients with hepatic disease, but a careful review of the literature has failed to reveal another reported case of viral hepatitis developing while a patient was taking anticoagulants. The patient under discussion was doing fairly well with prolonged anticoagulant therapy, despite infrequent medical visits and laboratory tests, until hepatitis developed. It was this complication that led to rapid potentiation of the anticoagulant effect, with bleeding and ultimate hospitalization. This case demonstrates the danger of anticoagulant therapy in the presence of hepatic disease and emphasizes the need for careful observation of patients receiving prolonged therapy.

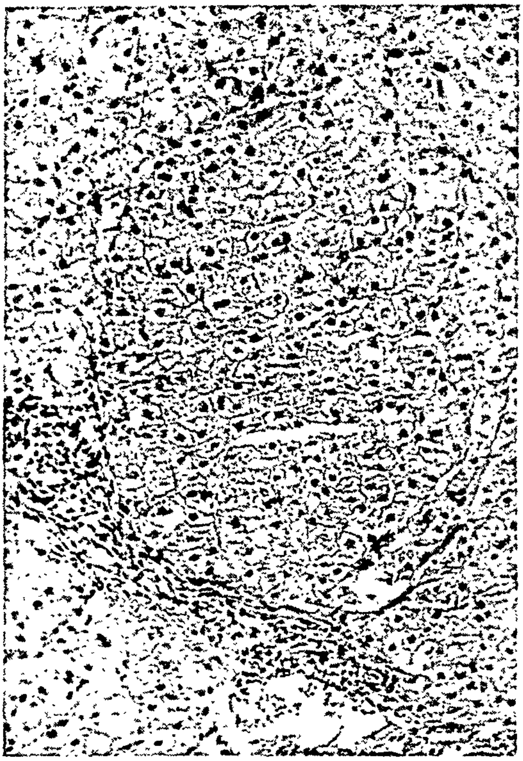

Fig. 3.—Liver biopsy section, 7/14/58: stromal collapse and scarring.

Summary

In this patient who had received prolonged anticoagulant therapy diffuse hemorrhagic manifestations developed after the onset of acute viral hepatitis. The tendency to bleed represented potentiation of the therapeutic effect of phenindione by intercurrent hepatitis.

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BRIEF PSYCHIATRIC APPROACH FOR THE CLINICIAN

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One of the most common objections to the evaluation and treatment of psychiatric problems that one hears from nonpsychiatric physicians and medical students is that psychiatry is too time-consuming. As a psychiatrist working and teaching in a busy medical clinic I have found this objection to be a valid one. The pressure of doing a comprehensive medical evaluation in as short a time as possible, with sufficient emphasis on the medical and psychiatric aspects, tends to make one seek more efficient methods. The psychiatric interview, as it is outlined in most textbooks, is too time-consuming for anyone but the psychiatrist. My experiences in the medical clinic have impressed me with need for developing a method of briefly evaluating and superficially treating psychiatric problems, especially such as are seen in the first interview when the diagnostic and therapeutic pressures are most severe. This paper deals with some but by no means all of the problems of brief psychiatric evaluation. This is not an ideal or complete method of handling emotional illnesses. It is a practical way

It is possible for even the busy family physician to gauge in a practical way the degree of a patient's neurosis. To estimate the patient's anxiety it is necessary to find out what the disease means to him; he may think of heart disease, for example, as synonymous with years of complete invalidism. To determine the relation of symptoms to the neurosis it is necessary to find out how the general course of his life has been altered by the symptoms; he may accept them with complacent inertia or react with constructive adjustments. A third factor to note is whether the patient gives his physician that minimum of cooperation needed to help him. Case histories illustrate these three points. Attention to them sometimes obviates the need for more time-consuming psychiatric interviews and helps the physician to evaluate, to treat superficially, or to decide whether further psychiatric help is needed.

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for the busy physician to measure the degree of neurosis, its influence on the illness, and the need for referral for proper psychiatric care or the necessity for therapy by the clinician.

Meaning of the Disease

First, it is important to recognize that all patients come to seek medical help because of anxiety about discomforts. If the patient were not anxious about his symptoms, he would not appear in your office. The physician should relieve the patient of his anxiety as well as treat the source of it; his success as a physician often hinges as much on how he handles the anxiety as on his skill at diagnosis and treatment. Although a calm and competent manner is usually sufficient, many patients also need some form of verbal explanation and reassurance. Too often this reassurance is so vague and general that it does not accomplish its purpose. When the patient is reassured as to specific fears, his fantasies are counteracted by facts, and at the same time the patient's trust in his doctor is augmented. Therefore, the physician must find out what the disease means to the patient.[1] Patients have not had the benefit of our training and experiences; therefore, diseases, technical words, signs, and symptoms may have entirely different meaning to them. The patient will evaluate any set of symptoms on the basis of a limited store of factual knowledge. Because of his limited contacts with the realities of the disease, the direction which the patient's fantasies will take is often determined by his personality and experiences.

An excellent example of this is the case of an active 54-year-old man who came into the medical clinic because of a mild cardiac condition of recent origin. His chief complaint was mild dyspnea; otherwise he was asymptomatic. It was noted that he was anxious and had severely limited his activity. He could not be reassured sufficiently to resume normal activity until we discovered that his mother had also had a cardiac condition and that she had been bedridden for many years. To this man cardiac disease was synonymous with complete invalidism. He had always been active and derived great pleasure from this. The idea of becoming dependent and inactive, and the memory of his mother's pain, filled him with terror. It was only when we were able to reassure him that his heart condition was not severe enough to require complete bed rest and that some activity was even desirable that much of his anxiety was dissipated. The cathartic effect of discussing his mother's disease and how he felt about it, and some additional factual knowledge about the heart, helped to treat the anxiety as well as the disease.

A few simple questions can usually help to evaluate the patient's anxiety. If he comes with a symptom for which he had no previous diagnosis, the questioning might develop in the following fashion.

Doctor: "What do you think is the matter?"

Patient: "I don't know."

Doctor: "Yes, I realize this, but what do you imagine is wrong?"

If the patient already has an idea of his own diagnosis one can omit this line of questioning and begin by asking such simple questions as, "What does [name of patient's presumed disease] mean to you?" "Have you ever known anyone with this condition?" "What do you know about it?" In a short time specific areas in which a patient needs understanding and help can be discovered. One must understand that every patient has fantasies about the etiology and significance of his symptoms but may be reluctant to speak about them and occasionally even to face them consciously.

Influence of the Disease

The next area to be examined is one which is based on the fact that most emotionally ill persons will use their symptoms in the service of their neurosis. It does not matter whether or not there is a specific organic abnormality; because the neurotic or psychotic handles the realities of life in an abnormal fashion, he will also tend to handle the realities of his disease with the same neurotic defenses. It is essential to know how the general course of the patient's life has been altered by this disease. Such a question as, "Would your life be very different if you did not have this condition?" usually gives the physician information in this area.[2] The emotionally ill patient answers that his life would be very different. The degree of difference measures the patient's "need" for the symptom and gives the physician an idea of how difficult it may be to remove the symptom. The 250-lb. (114-kg.) single girl who has no social life and stays home all day reading movie magazines and eating candy responds to this question by saying that if she were not fat she would be sociable, get married, and have children. Yet when one questions her further, it is easy to determine that all people make her anxious and that this is because she cannot tolerate the normal aggressions of everyday life. She is afraid of anything that has to do with sex. To this girl her obesity is a defense against facing aggression and sexuality. Actually, she feels relatively well emotionally when she is sickest physically.

The patient with the healthy personality will answer this question by saying that he continues to live in spite of his disease. Although his illness affects his life it does not stop him from living. An illustration of this is the 30-year-old man who became blind at the age of 20 with retinitis pigmentosa. Although he had no special financial assistance and came from a lower economic bracket, he was able to marry, to have children, and to support his family well. He was angry and at times depressed about his condition, but he had learned to live with and possibly in spite of his blindness.

The Doctor-Patient Relationship

My last point of evaluation does not require any specific questioning by the physician. It requires him to notice how the patient reacts to the situation in the physician's office. The doctor must realize that he is an important reality in the patient's life and that if the patient can deal with this reality normally he probably handles other situations in a similar fashion. What are the basic realities to which a patient must adjust in coming to the doctor? What is the minimum cooperation that we need in order to help patients? First, the patient must be able to communicate so that we can get an adequate history and physical examination. Second, he must be able to cooperate actively with the physician in his plan of management. Third, he must act in such a manner as to allow us to feel relatively comfortable in the practice of our profession. Naturally, we all treat patients who do not fulfill these criteria, but if a patient acts so as to interfere with our work and has no realistic reason for doing so, we should always suspect emotional illness.

A patient who dramatically illustrates some of the factors I have mentioned was one that I was called to see by a worried senior medical student. In a few minutes it was apparent why the student was so upset. The patient was a 44-year-old woman who was almost continuously moaning that her head hurt. Tears came to her eyes and she writhed on the table, clasping her head in her hands. To all of our questions she responded by saying that her head ached and she wanted treatment right away. We could not get her to answer simple questions and it took us at least five minutes to get her to sit up on the examining table. It was impossible to determine the duration, location, or quality of the pain. To all of our questions she replied with moans and pleas for help, but actually she interfered in our giving her help by not providing the minimum information necessary to treat her. I immediately left the room and called the patient's local physician, who knew her to be a neurotic person, with a drunken husband who would not support her and their five children. The patient had passively accepted this uncomfortable home situation for many years. I vigorously encouraged her to take some active control of her home situation, and gave her chlorpromazine (Thorazine) hydrochloride to help her control her inner turmoil. By the time of her next visit she was without pain and was taking steps to improve the situation which she had previously masochistically accepted. My interview with this patient did not take longer than 10 minutes. The main clue that helped me to realize that this was a neurotic patient was that she could not compose herself enough to help me understand a situation which she must have seen as life-threatening.

The following case shows how a patient's inability to follow the instructions of the physicians sometimes indicates serious mental pathology. A 56-year-old man gave a clear and detailed description of coronary heart disease, with occasional bouts of heart failure. His contact with reality appeared good until he began to describe taking digitalis for chest pain and not as routine daily medication. Questioning him further about this bizarre method of medication, I discovered a whole new area in the patient's life. Although leading a borderline existence and appearing relatively sane, he had grandiose delusions about himself. He believed that he had discovered a cure for cancer and rheumatoid arthritis. He was condescending toward all doctors and felt that he knew how to treat himself. We were never able to get this man to the state where he would take medicaments in the recommended doses because his delusions would not allow him to accept the word of any physician. He was given a diagnosis of schizophrenia, paranoid type. Again, the clue which led to the discovery of this psychosis was his inability to adjust to the realities of the doctor-patient relationship.

Comment.—All emotional illness is basically a result of abnormal handling of the conflict between personal needs and reality. Each person has a group of defense mechanisms which he uses to handle these conflicts. Such defense mechanisms are limited in number and are used in all situations. Therefore it can be said that the faulty defenses of a neurotic or psychotic patient will usually be present in the way he handles the realities of his disease or the doctor-patient relationship.

Summary

Three areas are to be investigated in the brief psychiatric evaluation: (1) what meaning the disease has to the patient, especially an evaluation of the anxiety associated with the illness; (2) how the patient's symptoms alter his life; and (3) how the patient adjusts to the reality of the therapeutic situation. Every physician realizes the importance of making a comprehensive evaluation of the patient in order to understand the complex interrelationships that influence the patient and his disease. Too often the busy physician is forced to neglect a psychiatric evaluation because of its time-consuming nature. This approach will help to obviate the problem.

2024 Delancey Pl. (3).

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TREATMENT OF SUPERFICIAL THROMBOPHLEBITIS WITH PHENYLBUTAZONE

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Phenylbutazone was used in the treatment of 40 patients with thrombophlebitis. The usual dosage schedule was 200 mg. by mouth thrice daily for three days and then 100 mg. thrice daily for four days. In each case the pain, swelling, and redness, and much of the induration, subsided promptly. The effects of the drug are illustrated by case histories of two men aged 20 and 27 years and a woman aged 27, chosen from the more difficult cases. Residual postphlebitic symptoms sometimes had to be controlled by the wearing of elastic stockings. No unfavorable side-effects from the drug were observed in any case.

In the medical management of thrombophlebitis, reliance has been almost completely on bed rest with elevation of the extremity, hot or cold applications, and anticoagulant therapy. Analgesics are frequently used to control pain, and antibiotics are used to combat the chills and fever which sometimes dominate the clinical picture. Given enough time, these measures will usually suffice in the resolution of thrombophlebitis in from one to four weeks. There is, however, a small but important group of patients in whom, despite such therapy, the disease remains active, causing much disability and economic loss.

Effectiveness

Because phenylbutazone had been found to bring prompt relief from acute inflammatory conditions such as rheumatoid arthritis and gout, it was given to patients with other inflammatory disorders. Its effectiveness in patients with thrombophlebitis was first reported by Dr. K. Sigg[1] in Europe and was confirmed by Dr. Irwin Stein[2] in New York. Dr. Stein began trials with this drug in 1954 on 33 patients with peripheral vascular disease, principally superficial phlebitis and varicose veins; also included were patients with thromboangiitis obliterans, migratory superficial phlebitis, and superficial phlebitis associated with malignant disease. The patients were ambulant, were not restricted in intake of salts, fluids, or diet, and received no treatment except with phenylbutazone. In all patients there was complete, rapid recovery from the venous inflammation.

In 1955 Dr. Stein[3] reported on 132 patients with superficial thrombophlebitis treated with phenylbutazone, with similar results. Later he induced venous thrombosis experimentally in rabbits[4] by injecting an irritant into the ear vein. He used three control groups; the first group received no treatment with phenylbutazone; the second group received phenylbutazone before injection of the irritant; and the third group received phenylbutazone after the development of thrombophlebitis. In the untreated group he observed the usual picture of progressive necrotic changes associated with the inflammatory reaction of thrombophlebitis. In the two groups treated with phenylbutazone the vein was protected from the irritant.

The mode of action of phenylbutazone is not completely understood. It has an analgesic action which is of a high order and is probably helpful in reducing the pain associated with thrombophlebitis. The antiphlogistic action of phenylbutazone is probably its primary function in the management of thrombophlebitis. It has been found that the combination of analgesic and anti-inflammatory actions is uniformly beneficial in the treatment of patients with thrombophlebitis. The pain, swelling, redness, and much of the induration in the superficial veins and adjacent tissues subsides within 24 hours in some and disappears within 72 to 96 hours in most patients. Of particular interest is the response in the treatment of thromboangiitis obliterans. It is probably the first time that such a specific phlebitis has been favorably influenced by medication.

Dangers

The frequently reported dangers in the use of phenylbutazone are real and must be stressed. The drug has been shown to have toxic effects on the marrow, with production of granulocytopenia, anemia, or both. Frequent blood cell counts should be made during the course of treatment. Because of the tendency toward gastrointestinal irritation and even hemorrhage, the drug should be given with or shortly after meals; the patient should be cautioned to watch the color of his stools and to discontinue use of the drug if vomiting or bleeding occurs. Skin eruptions are not uncommon. They are usually morbilliform in nature and tend to disappear on withdrawal of the drug. However there have been instances of severe dermatitis, some resulting in death due to exfoliation of the skin. The patient should be made aware of this possibility and advised to report any skin manifestation immediately. Phenylbutazone is, therefore, a drug to be used with caution and respect under any circumstances.

Under competent and constant supervision, particularly with short and limited periods of treatment, I believe this drug can be used with relative safety and that it may have an important place in the treatment of thrombophlebitis. The usual dosage schedule is 200 mg. of phenylbutazone three times daily for three days and then 100 mg. of phenylbutazone three times daily for four days. Rarely does this have to be repeated.

I had occasion to treat 25 patients with thrombophlebitis at the U. S. Army Hospital, Fort Sill, Okla., in 1956 and 1957 and about 15 patients in private practice since that time. All patients responded promptly to short courses of phenylbutazone therapy and no side-effects from the drug were observed in any. Three of the more difficult cases are presented.

Report of Cases

CASE 1.—A 20-year-old man, admitted to the Fort Sill Hospital in January, 1957, stated that while on leave he suddenly developed pain and swelling in the calf of his left leg, with subsequent development of pain in the left groin. He was hospitalized in the Veterans Administration Hospital in Des Moines, Iowa, for 30 days, during which time he received treatment including elevation of the extremity and use of elastic bandages, penicillin, anticoagulants, and sympathetic blocks. After 30 days the leg seemed to respond to treatment and the patient was discharged to return to Fort Sill. Four days after return to duty he noted the spontaneous onset of pain and swelling in the left calf; he was then admitted to my service. On examination I found a tender, erythematous, edematous left calf with tenderness in the popliteal space and along the saphenous vein of the thigh. The left thigh and calf were about 2 in. greater in circumference than the right. I treated the patient with the recommended dosage of phenylbutazone, and within 12 hours the pain had disappeared; in 36 hours all swelling had disappeared. The patient was allowed normal activity on the ward and did well except for the development of a minor postphlebitic syndrome shown by dependent rubor and slight edema of the foot after prolonged standing. This was easily compensated by an elastic stocking. The patient was seen repeatedly thereafter and three months later there was no evidence of recurrence of thrombophlebitis.

CASE 2.—A 27-year-old man was admitted in September, 1956, complaining of severe pain in the left arm. Close questioning revealed that his wife had playfully pinched his left biceps muscle three days prior to admission. Examination revealed that the patient was muscular, with a prominent, tender left brachial vein. The upper part of the left arm was 2 in. greater in circumference than the right. There was no evidence of puncture marks in the arm. He was treated with phenylbutazone alone and was asymptomatic within 24 hours. He returned to duty in seven days with apparently complete resolution of the phlebitic process.

Two weeks later he was readmitted with identical symptoms and findings as on the previous admission. No new injury could be found. A seven-day course of phenylbutazone again produced complete resolution of the disease, at which time he was again discharged and returned to duty.

Two weeks later he was readmitted with the same syndrome. Close questioning revealed that he wore tight T-shirts and worked on his back under vehicles with his arms extended upward in such a manner that the venous return was cut off between the tight T-shirt and the large biceps muscle. He was advised to wear loose clothing, and the thrombophlebitis did not recur.

CASE 3—A 27-year-old woman was first seen in May, 1958, with severe pain, swelling, and erythema of the right calf. She had been taking triamcinolone, 4 mg. three times daily, for several months because of a hyperhidrotic dermatitis of the hand. Administration of phenylbutazone was begun in the usual dosage, and in three days the condition of the leg was improved; however, improvement was not as great as had been anticipated. The dosage was decreased to 100 mg., three times daily, on the fourth day, but because of the slow response medication was continued for seven days instead of the usual four days, at which time all evidence of active disease had disappeared, but a postphlebitic syndrome had developed. The symptoms were controlled with an elastic stocking and have remained quiescent for almost a year. The slow response in this case may be attributed to the prolonged steroid therapy.

Comment

The advent of phenylbutazone in the treatment of thrombophlebitis offers much help in controlling a disease that has been marked by great frequency of recurrence and economic loss.

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TOTAL ADRENALECTOMY IN THE TREATMENT OF INTRACTABLE ASCITES

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Among patients in whom cirrhosis of the liver is accompanied by ascites there is a small group in whom the ascites cannot be abolished by the usual methods. Two patients of this type had failed to improve despite bed rest, diets low in sodium and moderately high in protein, intravenous administration of serum albumin, and paracentesis. In each case bilateral adrenalectomy was performed in two stages. In one case, that of a 50-year-old man, the interval between stages was 14 days; in the other, that of a 36-year-old woman, the interval was 12 days. The woman died two years later of delirium tremens but without recurrence of the ascites. The man made an excellent recovery. When ascites has proved intractable by the above criteria, the authors recommend bilateral adrenalectomy provided that the liver can reasonably be expected to regain some degree of functional competence.

Intractable ascites due to cirrhosis becomes a difficult problem for the internist who is treating it, as well as for the patient with this symptom complex. The theories of ascites formation in cirrhosis can usually be categorized into one of four categories: 1. It is due to portal hypertension and a weeping of the intestinal surfaces. 2. It is due to a weeping of the liver due to increased pressure within the lymphatics of the liver. 3. It is due to decreased protein formation because of a diseased liver with a resultant lowering of the serum proteins and the oncotic pressure within the circulating blood stream and, therefore, transudation of fluid into the peritoneal cavity. 4. It is due to retention of sodium as a result of abnormalities of hormonal systems.

With regard to the hormonal imbalance in ascites, clinical and experimental evidence has suggested that the cirrhotic liver favors the accumulation of antidiuretic substances.[1] For a time, attention was focused on ferritin, believed released in excess by the cirrhotic liver and thought to have an indirect antidiuretic effect through a trophic action on the posterior lobe of the pituitary. This mechanism has not been conclusively established.[2] More recently, failure of the cirrhotic liver to inactivate aldosterone, a strongly antidiuretic sodium-retaining hormone of the adrenal cortex, has been suggested by several investigators. There is evidence that aldosterone activity is increased in patients with cirrhosis.[3]

In ascites produced experimentally, Sprafka and others[4] and Davis and others[5] have shown that control of the ascites could be definitely obtained when the adrenal glands were removed. As a matter of fact, in an effort to obviate the necessity of replacement therapy, subtotal adrenalectomy was used by the former group and the ascites controlled without replacement therapy. Tewell and Freeman[6] have shown in animal experiments that adrenalectomy and hypophysectomy cause reduced excretion of corticoids and that these were probably of adrenal origin. Hamilton[7] has stated that the ascites occurring in dogs with mitral stenosis can be reversed with adrenalectomy.

Clinically, the treatment of cirrhotic ascites entails the use of bed rest, severe restriction of dietary sodium, vigorous administration of diuretics, diets moderately high in protein, intravenous use of serum albumin, and paracentesis. Androgenic steroids have been used to improve nitrogen balance. In spite of the successful management of a large group of patients by the aforementioned methods, there remains a small group with cirrhotic ascites that is truly intractable to treatment. Continued removal of fluid from the abdomen eventually drains the patient of much protein that is necessary for body function. This condition is as malignant as a malignant tumor. It will cause the patient's death.

When we were confronted with two such patients in the fall of 1956, bilateral adrenalectomy was elected because of our previous experimental results. Previous to the surgical treatment of these two patients, Marson,[8] and subsequently Giuseffi and associates,[9] reported similar experience in two cases. It is the purpose of this paper to report the effectiveness of bilateral adrenalectomy in the control of cirrhotic ascites and to give results of follow-up studies of these patients for the three years subsequent to the surgery.

Surgical Considerations

We have preferred a bilateral staged total adrenalectomy. This staged procedure is accomplished with about a 10-day interval between stages. Lat-

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eral decubitus position is preferred, with loin incision and extraperitoneal exposure of the gland. The approach to the gland is exactly the same as the approach to the kidney. Careful hemostasis is observed throughout. Drainage of the retroperitoneal area is obtained by the use of soft rubber drains. These are usually removed about the third or fourth day.

Preoperatively, the patient is given 300 mg. of cortisone daily for four days. This is continued between stages. After the second stage, the dosage of cortisone is slowly decreased over a period of 30 days to 25 mg. per day and adjusted more or less, depending on results of electrolyte studies and on physical needs. The conditions of both the patients mentioned in the reports have been maintained on therapy with 12.5 mg. per day, and the only salt restriction that is made is that of moderation.

We should like to emphasize the benignity of the patient's course during and after operation. Food is allowed on the second postoperative day and thereafter. The diet, which at first is a continuation of the low-salt diet, is gradually changed over a period of 30 days to regular diet with little or no salt restriction. With regard to preoperative paracentesis, we have utilized this to facilitate ease of induction of anesthesia, which could be hindered by the presence of an elevated diaphragm.

Report of Cases

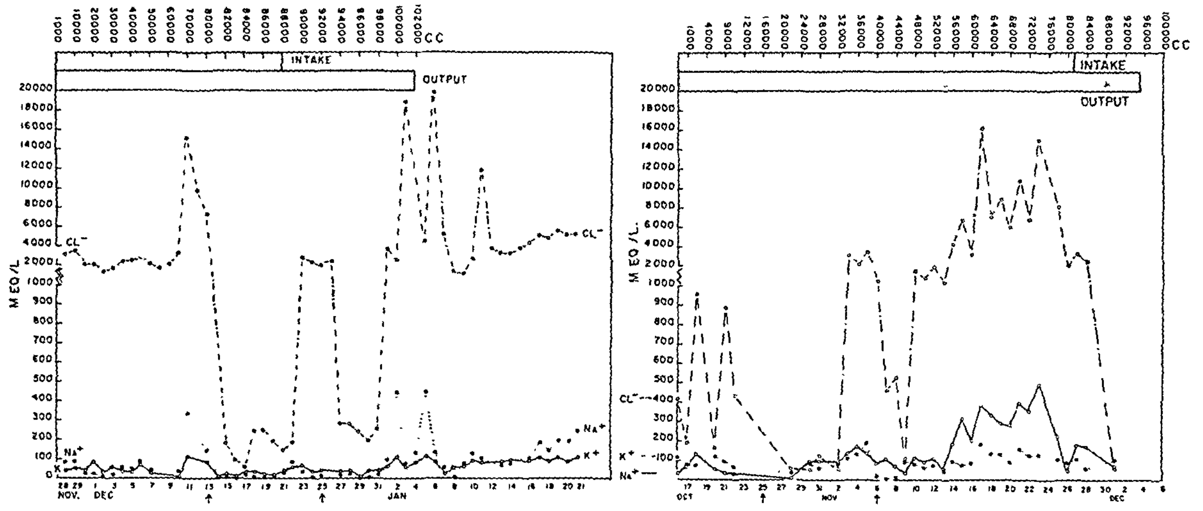
Case 1.—A 50-year-old man was admitted to the hospital, Nov. 26, 1956, complaining of abdominal distention. He had been a heavy and steady user of alcohol for at least 10 years. In 1952, he had been hospitalized because of nausea, anorexia, and malaise and had been treated with a number of blood transfusions. In 1954, he was hospitalized because of ascites, and a diagnosis of Laennec's cirrhosis was established. He was treated with controlled diet, rest, and paracentesis. In the interim he had not been well and a paracentesis had been required about every two weeks until eight months before the present admission. At that time he had been placed on a low-sodium diet and was given ammonium chloride and mercurial diuretics; while further paracentesis had not been necessary, the abdomen remained distended. He had not had hepatitis, jaundice, or hemorrhage. The total number of paracenteses throughout the hospital stay was 39. A review of systems gave essentially negative information, except as described above. History revealed the usual diseases of childhood, diphtheria, and syphilis in 1937, with six months of therapy. He had a hemorrhoidectomy in 1951.

Examination revealed a well-developed, fairly well-nourished, middle-aged male with obvious ascites; he appeared to be chronically ill. The vital signs were normal and included a pulse rate of 76 per minute and blood pressure of 106/62 mm. Hg. His weight was 162 lb. (73.5 kg.). Significant findings included a few spider hemangiomas on the anterior part of the thorax and hepatomegaly, with the liver edge extending 5 cm. below the right costal margin. The spleen was not palpable and there was no dependent edema.

Laboratory studies revealed the following data: serum protein level, 7.6 Gm.%, with an albumin-globulin ratio of 3.5/4.5; prothrombin level, 77% of normal; sulfobromophthalein retention, 2.5% at 45 minutes; cephalin flocculation, 3+ at 48 hours; serum bilirubin level, 0.25% mg.; and thymol turbidity 3.2 units. The hematocrit value was 59%, and the circulating blood volume was 88 ml. per kilogram of body weight. The serum sodium level was 139 mEq. per liter and potassium level 5.1 mEq. per liter. The urine contained 72 mEq. per liter of sodium and 44 mEq. per liter of potassium. The amount of sodium chloride excreted daily was 5 to 6 Gm., on a low-sodium diet. After several months of conservative management with a diet high in protein and low in sodium, moderate doses of testosterone, mercurial diuretics, and frequent paracentesis, it was concluded that the ascites was "intractable."

On Dec. 7, 1956, the patient was started on therapy with cortisone, in preparation for a two-stage adrenalectomy. On Dec. 12, 1956, 7,140 ml. of ascitic fluid was obtained by abdominal paracentesis. Adrenalectomy on the right was performed on Dec. 13. The gland weighed 16 Gm. and appeared normal on gross and microscopic examination. On Dec. 25, 1956, after paracenteses of 4,140 ml., an adrenalectomy was performed on the left. The gland weighed 7 Gm. and appeared normal on gross and microscopic examination. The patient withstood the operative procedure well, and the postoperative course was not complicated. The cortisone dosage was gradually reduced from 300 to 25 mg. per day during the first 30 days of convalescence. On the 18th postoperative day, the serum sodium level was 130 mEq. per liter and the potassium level 5.9 mEq. per liter; the urine volume was 2,500 ml. and contained 68 mEq. per liter of sodium and 34 mEq. per liter of potassium. The patient was discharged from the hospital Jan. 23, 1957, improved, with activity at about the same level as on admission, and on a normal diet, with unrestricted sodium intake.

He has continued to do well except for one occasion about three months after discharge from the hospital. At that time he was readmitted because of a reaccumulation of a small amount of ascites after the ingestion of a large amount of salt contained in ham and bacon. His weight was 154 lb. (70 kg.). Liver function studies gave the following data: bilirubin level, 0.75 mg.%; cephalin flocculation, 4+ (48 hours); alkaline phosphatase level. 3.8 units (Bodansky method); total serum protein level, 7.8 Gm.%; albumin-globulin ratio, 3.9/3.9; sulfobromophthalein retention, 5.5%; and prothrombin time, 76%. The patient's course was uneventful and was remarkable in that the ascites cleared readily in a matter of four or five days on a 500-mg. sodium diet alone. This was impossible prior to the adrenalectomy. The patient was discharged on a regular salt diet.



Charts show urinary sodium, chloride, and potassium excretion values. Arrows point to date of surgery. Note increase in sodium excretion after removal of second adrenal gland.

He was next seen on Feb. 9, 1959. His condition had been maintained on 12.5 mg. of cortisone daily, one tablet of methyltestosterone (Metandren) daily, and 50 mg. of vitamin C three times every day. There was no evidence of ascites. His weight was 184 lb. (83.5 kg.), the build was solid, and there was an increase in arm and chest girth. He had been feeling exceptionally well. On Nov. 25, 1958, the urinary ketosteroid excretion value was 8 mg. per 24 hours. The 17-ketogenic steroid excretion value was 10 mg. per 24 hours. On April 14, 1959, the 17-ketosteroid value was 4 mg. per 24 hours and the 17-ketogenic steroid value 10 mg. per 24 hours. This is just accounted for by the dosage of cortisone. It is important to note that specimens collected on March 17 and March 22, 1959, showed no evidence of aldosterone in the urine. Laboratory studies on Feb. 9, 1959, showed a prothrombin time of 100%; sulfobromophthalein retention, 5.5%; cephalin flocculation 2+ (48 hours); serum sodium level, 140 mEq. per liter; and serum potassium level, 5.5 mEq. per liter. He has had an excellent result.

Case 2.—A 36-year-old woman was admitted to the hospital on Sept. 20, 1956, because of recurring ascites of seven months' duration. She had been a heavy user of alcohol for many years and first had been hospitalized for uncompensated cirrhosis in 1950. She had required hospitalization repeatedly for jaundice and ascites, and her condition was deteriorating rapidly. There were no symptoms except those of the gastrointestinal system. She had had dark stools six years before and cirrhosis as noted above. Her history revealed the usual diseases of childhood but no other pertinent information.

Examination revealed a cirrhotic female, with a protuberant abdomen, who appeared much older than the stated age and chronically ill. Her height was 61 in. (155 cm.), weight 140 lb. (63.5 kg.), pulse rate 120 per minute, and blood pressure 126/76 mm. Hg. She was afebrile. Significant deviations from the normal were ascites and smooth but enlarged liver extending 5 cm. below the right costal margin. The spleen was not palpable and there was no dependent edema.

Supplemental studies revealed a serum sodium level of 136 mEq. per liter; potassium level, 412 mEq. per liter; urine volume, 1,930 ml. per day, with sodium level of 143 mEq. per liter and potassium level of 5.1 mEq. per liter. The total serum protein level was 7.8%, with an albumin-globulin ratio of 4.3/3.6 and 17-ketosteroid output of 15 mg. per day. The prothrombin level was 60% of normal; sulfobromophthalein retention 21% at 45 minutes; cephalin cholesterol flocculation 2+ at 48 hours; serum bilirubin level 75 mg.%; and thymol turbidity 1.7 units. Results of other laboratory studies did not deviate from normal.

The patient was treated with a program similar to that of the first patient. On the fourth hospital day, 14,000 ml. of ascitic fluid was obtained by paracentesis. After the patient had been prepared with cortisone therapy, adrenalectomy on the left was performed on Oct. 25, 1956, and on the right on Nov. 6, 1956. The glands weighed 8 and 18 Gm., respectively, and appeared normal grossly and microscopically. The cortisone dosage was reduced from 300 to 25 mg. daily during the next 34 days. The patient was fed a diet with no sodium restriction. On the 20th hospital day, the serum sodium level was 142 mEq. per liter and the potassium level 5.3 mEq. per liter. The quantity of urine produced that day was 3,000 ml., and it contained 160 mEq. per liter of sodium and 45 mEq. per liter of potassium. She improved notably after the operation, gained weight and strength, and had the appearance of good health. She was discharged on Nov. 28, 1956. She required no mineral corticoids. On Dec. 17, 1956, in the course of a respiratory infection, she developed nausea and vomiting and was admitted to the hospital. The vital signs were, however, normal, with blood pressure of 120/70 mm. Hg. She was not dehydrated and she did not require emergency measures for hypoadrenocorticism. The regimen was not changed, except that palliative measures were given for the respiratory infection and an antibiotic was given. She was discharged after three days. During May and June, 1957, she had 12 teeth extracted in three sittings as an outpatient. For these procedures the cortisone dosage was increased to 100 mg. daily, and the patient was given penicillin prophylactically. She withstood these procedures well and had no complications. Urinary aldosterone determinations, at that time, showed negative results. When last seen on May 21, 1958, she was eating a regular diet, with salt as desired. She received 25 mg. of cortisone and 150 mg. of ascorbic acid daily. She had no evidence of ascites. The hepatic function was approaching normal. She looked very well, weighing 120 lb. (54.4 kg.) at that time. She failed to keep scheduled appointments, but her husband kept us informed. She apparently returned to drinking heavily, but in spite of that she appeared very well with no apparent ascites. She kept on taking essential medicaments.

In the early part of November, 1958, she was admitted to a psychiatric hospital because of several episodes of delirium tremens. While there she became markedly jaundiced and died of hepatic coma. A postmortem examination was performed. This, essentially, revealed terminal bronchopneumonia, 2 liters of fluid in the abdomen, and far-advanced Laennec's cirrhosis with minimal pericholangitis. Essentially, this patient had a good result with death due to a return to severe alcoholism.

Comment

It is conceded that the obvious treatment in cirrhotic ascites would be the treatment of the cirrhosis itself, just as it would be in those cases in which portacaval shunts are done for bleeding due to the cirrhosis and portal hypertension, but, until the day comes when actual treatment and cure of cirrhosis is possible, treatment of the disturbed pathological physiology resulting from cirrhosis is in order. It is also conceded that adrenalectomy is a rather vigorous approach to the problem of ascites, but it must be also realized that intractable ascites can cause the death of a patient and, therefore, must be treated radically. It is not suggested that adrenalectomy be done for those patients for whom other methods of control can be effectively used. On the other hand, the so-called conservative treatments, such as low-sodium diet, are not without their drawbacks. It is easy for a physician to recommend a low-sodium diet to a patient, but our experience has been that low-sodium diets of the magnitude necessary to control ascites are, in fact, rather radical treatments. The patients complain bitterly about the tastelessness of the food and in many instances manage to "smuggle in" a bit of salt in their diet.

A program that would permit a diet with little or no salt restriction would be a great asset. It was with this in mind that the adrenalectomies were done. Whether or not aldosterone destruction takes place in the patient with cirrhosis is not immediately pertinent to this paper. It would serve as an interesting problem for the future. Certainly, a substance that would act as an antialdosterone and could be taken by mouth or by injection would be desirable, if aldosterone were the involved substance in ascites. Such a substance, 1,2-bis(p-aminophenyl)-2-methylpropanone-1 (Amphenone), has recently been reported, but the effectiveness of its administration has not been shown clearly and it is quite toxic, especially to the central nervous system. Certainly, the future holds the promise of such a substance being developed, and this, of course, would obviate the necessity for adrenalectomy, if the aldosterone fraction is the involved substance.

It is interesting to note that the required replacement therapy is so low. It was thought at first that it might be higher than this, as pointed out by Hills and associates [10] in his group of patients with adrenalectomy for hypertension. These patients should be forewarned that, under certain conditions of stress, such as a cold or the extraction of teeth, an increased dosage of cortisone is necessary. They must, therefore, return to their physicians and have the dosage readjusted for a short period of time. Under these circumstances, there is no reason to believe that these patients cannot continue living in a normal fashion, except for taking a pill every day.

It is interesting to note that both of the patients were gaining weight that was not considered to be the result of fluid formation. Apparently, the protein that was lost with the ascites was now being reutilized by the body instead. These patients seemed to have much more energy and were able to partake of their normal activities. With regard to the technique of the adrenalectomy itself, it is also interesting to note that the two-stage adrenalectomy rather than the single-stage bilateral adrenalectomy was effective and of little trauma to the patients. These patients were able to eat on the day after the initial operation, with little effect due to the operation itself. Ten days after the initial adrenalectomy, the other stage is accomplished, and again the patients recover very rapidly. On the other hand, it has been our experience that a one-stage bilateral adrenalectomy is a much more shocking procedure, with an increased morbidity and mortality. It is, therefore, suggested that in cases in which adrenalectomy is contemplated for this condition, a two-stage procedure be undertaken.

A recent experience at the Mount Sinai Hospital in which a patient died of his disease while he was being prepared for surgery has led to a suggestion that in such cases liver biopsy is in order. A postmortem examination performed on this patient disclosed hepatoma, which caused the death and which in all probability would have caused an undesirable result after adrenalectomy. In other words, the life span of the patient would not have been prolonged by the procedure. It is, therefore, suggested that a liver biopsy specimen be obtained prior to adrenalectomy in order that it be established that cirrhosis is of the Laennec type.

It is also important to note that in both patients reported here an increase in the urinary sodium excretion level was noted after adrenalectomy. This, undoubtedly, was related to the absence of circulating aldosterone. However, it must also be noted that, in spite of no evidence of aldosterone, these patients can and will accumulate sodium if it is available to the body in more than the usual amounts that one eats in a regular diet (case 1). Apparently these patients are different than those patients who undergo adrenalectomy for cancer.[11]

Summary and Conclusions

Bilateral adrenalectomy was performed on two patients with intractable ascites due to Laennec's cirrhosis. These patients were followed up for periods of two and three years respectively. There was a striking increase in urinary sodium excretion in both cases. In spite of evidence that the amount of aldosterone is greatly decreased or absent, unusual amounts of salt intake will cause sodium retention that will respond easily to decrease in salt intake. On ordinary salt intake, ascites does not recur. It is believed that bilateral adrenalectomy is a valuable addition to the therapeutic management of patients with intractable ascites due to hepatic cirrhosis under the following circumstances: (1) evidence of a favorable prognosis of the cirrhosis itself, i. e., a reasonable expectation of some reversibility, (2) absence of esophageal hemorrhage, varices, or other evidence of far-advanced portal hypertension, (3) absence of marked hypoproteinemia or favorable response to measures directed at restoration of normal serum protein levels, and (4) failure of response to dietary sodium restriction and administration of diuretics.

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THE RETROGRADE SPREAD OF EXPERIMENTAL CARCINOMA IN RABBITS.—Retrograde spread of cancer in the lymphatic system is seen experimentally, as it is seen in man. Such spread may occur as early as 6 weeks after the introduction of tumor into the lymphatic system. Early tumor growth in the retrograde node occurs usually in the subcapsular sinus region, and infrequently in the medullary region. Tumor cell emboli pass backward through circuitous collateral lymphatics which empty into afferent lymphatics of the retrograde node. These afferents then carry the emboli forward to the subcapsular sinus.—I. Zeidman, Experimental Studies on the Spread of Cancer in the Lymphatic System, *Cancer Research*, November, 1959.

CLINICAL NOTES

RETROGRADE PYELOGRAPHY AND USE OF CONTRAST MEDIUMS CONTAINING NEOMYCIN

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The practice of making retrograde pyelographic studies with use of radiopaque mediums was first suggested by Von Lichtenberg and Voelcker[1] in 1906. Since then many kinds of iodine derivatives have been tried, some of them toxic to the subject, until the use of sodium iodide in 10 to 12% solution was established as being free from danger. The modern type of contrast medium dates from a little more than a decade ago, and each year since then has seen new products presented to the medical profession. Recently, experiments were performed with products containing determined percentages of antibiotics in an attempt to avoid reactions that occur after retrograde pyelography, which sometimes assume serious proportions. But perhaps it would be of greater avail to reconsider basic principles of technique than to rely on covering up the damage with antibiotics. In this regard, we should like to relate some personal observations.

It is our impression that there is no difference in result (regarding reactions after retrograde pyelography) whether the gravity instillation method with the patient in the Trendelenburg position is employed or a slow injection of medium is carried out with the patient in the horizontal position. A sensation of fulness in the flank may be considered normal, but one should not have to depend on colic to realize that sufficient medium has been instilled. The overdistention of the pelvis is probably responsible in most patients for the immediate reaction of pain in the kidney area. It is true that spasm of the collecting system in reacting to the irritant action of some contrast mediums may be a component of importance, but this seems to occur when reinjection has been done in order to obtain films of better diagnostic quality.

Various textbooks of urology suggest unduly large quantities of contrast medium as proper for instillation (for example, 8 to 15 cc. by Campbell,[2] 8 to 10 cc. by McCrea,[3] 7.5 to 20 cc. by Wesson and Ruggles[4]). This is most unfortunate, since pursuing this practice invariably will lead, in a renal pelvis of normal capacity, to the "overdistention reaction." In the vast majority of our adult patients, in whom hydronephrosis or pyelectasis was not previously suspected, 2.5 to 3.0 cc. of contrast medium was adequate to obtain the desired delineation of the collecting system. Larger amounts would in many cases mask minor details, distend calyces, and produce pyelovenous or pyelolymphatic reflux as well as pain.

The delayed reaction from retrograde injection of contrast medium, characterized by bacteremic chills and fever, is unnecessarily common and is the feature which prompted the latest study with a medium containing antibiotic material. While such a reaction may result from impaired drainage associated with urinary tract infection, it is our feeling that in "normal" situations it occurs because of overinjection. The usual adult renal pelvis is not prepared to accept more than 3 cc. In children 2 cc. should be maximal and in infants 1 cc.

Our controlled studies in two consecutive series of 100 patients each showed no clinical difference between the simple contrast medium (methiodal sodium) and the one containing 2.5% of neomycin sulfate. We observed two bacteremic episodes in each of the groups, and the patients in whom they occurred required supplementary administration of antibiotics during the peak of the crisis. The reactions occurred in patients in whom reinjection was done to obtain a ureterogram, study drainage time in cases of ureteropelvic junction obstruction, or find out the exact amount necessary to fill a hydronephrotic kidney. The diagnostic quality of the films was identical in both series.

Conclusions

The prophylactic or therapeutic value of the addition of neomycin sulfate to opaque mediums seems insufficient to justify its use at an increased cost. Reactions after retrograde pyelography would be more apt to be prevented if textbooks accurately stated the anatomic capacity of the renal pelvis and if this were heeded by the cystoscopist.

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The material used in this study was supplied by Winthrop Laboratories, New York, through Mr. Shepherd Crain of the Department of Medical Research.

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AGRANULOCYTOSIS DUE TO ADMINISTRATION OF SALICYLAZOSULFAPYRIDINE (AZULFIDINE)

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Salicylazosulfapyridine (Azulfidine) is an azo compound of salicylic acid and sulfapyridine first introduced in 1942 by Svartz[1] for the treatment of ulcerative colitis. In the early clinical trials with this medicament hypersensitivity reactions, particularly drug fever and rash, were noted in about 5% of patients.[2] Five instances of leukopenia were observed but no cases of agranulocytosis or nephrolithiasis. Bargen,[3] Morrison,[4] and others[5] have also noted the usefulness of salicylazosulfapyridine and its low incidence of hematological complications.

The first reported instance of agranulocytosis after the use of salicylazosulfapyridine was described by Levy in 1949.[6] His patient recovered from a complicating staphylococcic septicemia after treatment with penicillin. We are aware of only one other occurrence of agranulocytosis associated with administration of this drug.[7] In view of the extensive use of salicylazosulfapyridine in the treatment of patients with ulcerative colitis, the following case of agranulocytosis is reported to emphasize the need for hematological surveillance when administering this drug.

Report of a Case

A 58-year-old man was first seen on Dec. 19, 1958, because of bloody diarrhea during the previous four weeks. The sigmoidoscopic examination revealed an ulcerated granular mucosa which was friable and bled easily. A mucopurulent bloody discharge was present. Examination with an air-contrast barium enema did not indicate any disease in the remaining portion of the colon. The findings were characteristic of ulcerative colitis.

The patient was placed on a milk-free diet and given salicylazosulfapyridine in a dosage of 1 Gm. four times daily. Four days later a generalized rash was noted. The medication was discontinued for four days, at which time the rash had disappeared. The patient was then given salicylazosulfapyridine therapy again, 3 Gm. daily, without any observable ill-effect. He also received a multivitamin capsule daily as well as a protein supplement. On this regimen the bowel movements improved with respect to urgency, frequency, and bleeding. The patient gained weight.

Blood tests made on Dec. 30, 1958, showed the following values: hemoglobin concentration 12.8 Gm.%; red blood cell count 4,210,000 per cubic millimeter; white blood cell count 4,350 per cubic millimeter, with 53% polymorphonuclear cells, 2% band forms, 34% lymphocytes, 9% monocytes, and 2% eosinophils. The platelets were normal on smear. Another sigmoidoscopic examination at this time showed diminution in the friability and ulceration of the mucosa. The purulent discharge had disappeared. However, there was still considerable inflammation and edema of the intestine. The patient was therefore given 20 mg. of prednisolone daily in addition to salicylazosulfapyridine.

During the next two weeks there was further clinical and sigmoidoscopic improvement. On Jan. 20, 1959, he began to complain of severe exhaustion and anorexia. He collapsed at work on Jan. 23 and was admitted to the hospital. Administration of salicylazosulfapyridine was discontinued.

On admission, he appeared to be a well-developed, lean man, not acutely ill. His temperature was 102 F (38.9 C), and his pulse was 92 per minute. No ulcerations were noted in the mouth or pharynx. The heart and lungs were normal. The liver edge was just palpable; the spleen and lymph nodes were not enlarged. The initial blood studies showed a hemoglobin concentration of 13.2 Gm.%; white blood cell count was 1,300 per cubic millimeter, with 98% lymphocytes and 2% monocytes. No immature cells or granulocytes were seen. The platelets appeared adequate in number. A urinalysis revealed a specific gravity of 1.012 and did not show sugar or albumin; the microscopic examination was not remarkable. Result of the Mazzini test was negative. The blood urea nitrogen level was 22 mg.%. Icterus index was 4. The cholesterol level was 180 mg.%; cephalin flocculation negative; thymol turbidity 2 units; alkaline phosphatase level 5.5 King-Armstrong units; and acid phosphatase level 1.7 units. The total serum protein level was 6.3 Gm., including 2.7 Gm. of albumin and 3.6 Gm. of globulin. A fractionation of the globulin indicated 36.5% alpha, 4.8% beta, and 15.9% gamma globulin. The prothrombin time (Quick) was 14 seconds, as compared to a control of 12 seconds. A blood culture taken on Jan. 25, 1959, was normal. Agglutination studies for enteric fevers also gave normal results.

A marrow aspiration was performed on Jan. 24, 1959, from the right iliac crest. Many spicules were obtained. The stroma was vacuolated and empty (fig. 1). No myeloid elements were seen. The remaining cells consisted mainly of lymphocytes and plasma cells. Occasional nests of normoblasts were seen as well as an infrequent megakaryocyte. The interpretation was agranulocytosis and hypoplasia of the marrow.

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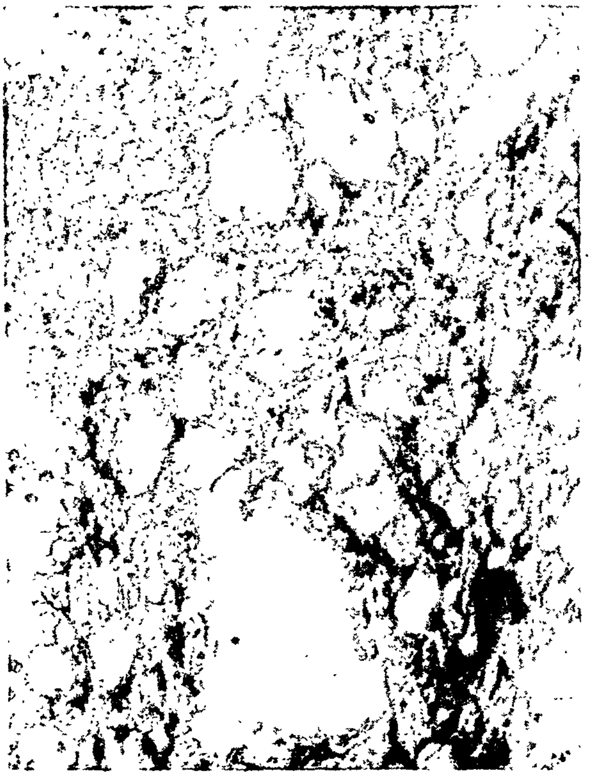

Fig. 1.—Marrow spicule in hypoplastic phase, showing empty marrow (× 100).

The patient was treated with penicillin, 600,000 units intramuscularly every six hours, and prednisone (Meticorten), 5 mg. 3 times daily. He continued to run a febrile course, with temperatures up to 103 F (39.4 C) during the first eight days of his hospital stay. The hematological data are summarized in table 1. On Jan. 30, 1959, because of his poor progress, the dose of prednisone was increased to 40 mg. daily. The next day the patient was afebrile for the first time and began to improve rapidly thereafter.

Another marrow aspiration was obtained from the same iliac crest on Feb. 5. There was moderate hypocellularity, as compared to the normal. However, there were now many myeloid cells in all stages of development, with a shift to the left. A third marrow aspiration from the same site on Feb. 13 showed a hyperplastic marrow and full recovery of myelopoiesis (fig. 2).

The dosages of penicillin and prednisone were gradually decreased as the patient improved clinically. On Feb. 9 administration of penicillin was discontinued. The patient was discharged a week later, taking 5 mg. of prednisone four times daily. His condition was much improved, but the ulcerative colitis was still active. When rechecked two weeks after his discharge he had made a complete hematological recovery.

Leukocyte Agglutinin Studies.—Studies of leukocyte agglutins in this patient were performed by the method of Schwartz and Hass.[8] This is a modification of the procedure described by Dausset and co-workers,[9] in which a suspension of blood-group compatible, normal leukocytes is incubated with the patient's inactivated serum. The white blood cell suspension is then examined microscopically for agglutination and graded from +1 to +4.

Tests of the patient's serum during the period of granulocytosis did not reveal a leukoagglutinin. Since this test was made 12 days after administration of salicylazosulfapyridine had been discontinued, it was repeated after addition of 0.1 cc. of a dilute solution of salicylazosulfapyridine (0.5 Gm. of salicylazosulfapyridine dissolved in 100 cc. of distilled water and filtered to give a clear solution) to the incubation mixture with use of a normal control. Leukocyte counts were done in duplicate on the resulting suspension. The results, which are given in table 2, show that when salicylazosulfapyridine was added, there was a significant reduction in the number of leukocytes remaining in the suspension with the patient's serum. A normal control showed only one-third as much of a decrease.

Comment

The occurrence of agranulocytosis due to "sulfa" drugs has been well documented. Therefore it is not surprising that salicylazosulfapyridine, a sulfonamide derivative, may produce this condition. Because of the paucity of reported cases, in the face of the widespread use of the drug, its incidence must be rare.

TABLE 1.—*Hematological Data on Patient with Agranulocytosis*

Date, 1959	Hemoglobin Concentration, %	Platelets, × 1,000	White Blood Cells, × 1,000	Myeloblasts	Premyelocytes, %	Myelocytes, %	Metamyelocytes, %	Band Forms, %	Polymorphonuclear Cells, %	Basophils, %	Lymphocytes, %	Monocytes, %
1/26	12.5	120.0	1.20	..	..	..	..	..	..	..	98	2
1/28	12.5	174.0	1.20	4	..	..	..	..	..	..	46	..
1/30	11.7	....	1.65	..	..	..	..	...	..	..	..	..
2/2	11.9	192.0	5.45	5	2	13	11	25	13	..	15	15
2/3	12.5	....	9.30	..	..	..	..	..	..	..	..	..
2/5	12.5	800.0	22.80	16	5	9	13	14	35	..	5	3
2/6	12.1	692.0	28.10	..	..	..	..	..	..	..	..	..
2/9	12.1	618.0	26.30	2	1	2	9	14	62	..	6	4
2/11	11.3	600.0	15.20	1	..	1	1	17	65	1	8	6
2/13	11.6	592.0	13.70	..	..	..	2	13	60	1	18	6
2/28	14.0	300.0	7.80	..	..	1	..	..	77	..	22	..

The patient described here had a transitory skin rash four days after therapy with salicylazosulfapyridine was started, in a dosage of 4 Gm. daily. The rash cleared rapidly and did not recur after the medication was reinstituted at a lower dosage. Such manifestations of idiosyncrasy as urticaria, edema, and asthma frequently occur with drugs which may produce agranulocytosis in man.[10] The occurrence of a drug rash due to a sulfonamide should be a contraindication to readministration of the drug.

The mechanism of agranulocytosis may be one of "maturation arrest" in the marrow, wherein the marrow is cellular and shows a predominance of young myeloid forms but no mature segmented cells. However, more emphasis is now placed on the concept of a circulating leukoagglutinin or toxic agent.[11] There is increased peripheral destruction of leukocytes, producing an increased demand on the marrow, with early decrease of mature forms and hyperactivity of the granulocytic series. When leukocyte destruction is protracted, myelopoiesis may be exhausted and an aplastic reaction may ensue.

When the marrow begins to recover, immature cells are poured into the peripheral blood as occurred in this patient, and a leukemoid reaction may be simulated. The leukocyte count can rise to high levels and many young forms may be seen. In another case of agranulocytosis produced by administration of chloramphenicol (Chloromycetin), which was studied by one of us (N. D. R.), the leukocyte count rose to 65,000 per cubic millimeter during the recovery phase. The platelets may share in this exuberant outburst. Our patient's platelet count reached 800,000 per cubic millimeter as he was improving.

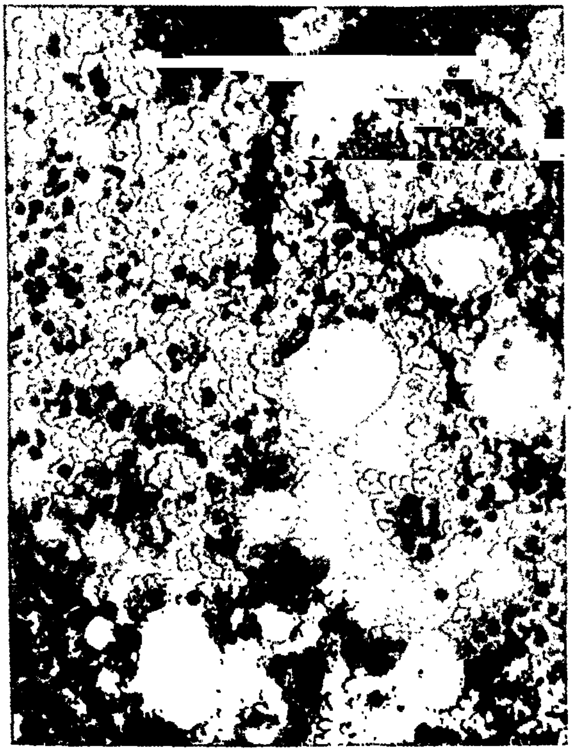

Fig. 2.—Marrow spicule in recovery phase, showing hyperplastic marrow (× 100).

The interpretation of the leukocyte studies is difficult. The result of the leukoagglutinin test as usually performed was negative on two occasions. When the test was modified, with the leukocytes counted in the incubated mixture of patient's serum leukocyte suspension and salicylazosulfapyridine solution, a lower white blood cell count was found than in a similarly constituted control. Thus the leukocytes were lysed in the presence of the patient's serum plus the active haptene, salicylazosulfapyridine. This observation is similar to that of the antibody system against platelets demonstrated by Ackroyd[12] in the serum of persons sensitive to allyl-isopropyl-acetylcarbamide (Sedormid). Tullis[13] in a like manner has used a lysis index to study leukocyte antibodies by noting the percentage decrease in motile leukocytes after incubation with the test serums. The evidence would therefore indicate that an antibody which destroys leukocytes may be elaborated by a patient sensitive to salicylazosulfapyridine.

TABLE 2.—*Leukocyte Count per Cubic Millimeter of Incubation Mixture of Leukocytes and Patient's Serum*

	With Saline Solution	With Salicylazosulfapyridine Solution
Patient	950	350
Normal control	950	750

Summary

In a case of agranulocytosis due to administration of the sulfonamide salicylazosulfapyridine (Azulfidine) a leukemoid reaction occurred during the recovery phase. The agranulocytosis produced by salicylazosulfapyridine may have been due to the formation of an antileukocyte antibody.

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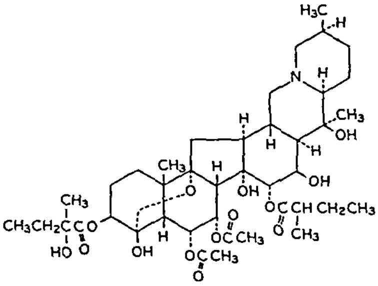
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Protoveratrine A (Protalba).—Protoverine 3-(*d*)-2-hydroxy-2-methylbutyrate 6,7-diacetate 15-(*l*)-2-methylbutyrate.—The structural formula of protoveratrine A may be represented as follows:



Actions and Uses.—Protoveratrine A, which has actions, uses, and side-effects that resemble those of the preparation protoveratrines A and B, is employed clinically in the management of hypertension. Protoveratrine A differs chemically from protoveratrine B only by one additional oxygen atom; the pharmacological effects of the two alkaloids are qualitatively similar. Quantitatively, protoveratrine A is the more potent. Although the exact relative oral potency of the two drugs in man remains to be established, the available evidence suggests that protoveratrine A may be up to 10 times as active as protoveratrine B. On the other hand, on intravenous injection in dogs, the two alkaloids have approximately the same hypotensive activity, protoveratrine A being only slightly the more potent.

Protoveratrine A is employed for the adjunctive management of hypertension in the same manner as the preparation protoveratrines A and B. Although it is effective in lower doses than the latter preparation, the margin between the effective antihypertensive dose and the emetic dose is no greater. Consequently, protoveratrine A shares the major disadvantage of other Veratrum preparations; doses only slightly greater than those required for therapeutic action produce vomiting and other unpleasant effects. Dosage, therefore, must be regulated with the greatest precision. Protoveratrine A has the advantage that it is a single alkaloid and not a complex product containing two or more alkaloids whose proportions may vary in different preparations. However, the superiority of the single alkaloid over other well-standardized Veratrum preparations is largely theoretical and has not yet been demonstrated in the clinic.

Dosage.—Protoveratrine A is administered orally, usually after meals and at bedtime. The principles of dosage are the same as for the oral administration of protoveratrines A and B. Because the margin between the effective and toxic doses is, in many patients, quite small, successful use of the drug depends on individualization of the dose. Hospitalization of the patient facilitates determination of the optimal dosage schedule. If possible, the blood pressure should be determined two to three hours after each dose as a guide to appropriate dosage adjustments. The patient should be instructed to report the earliest symptoms of toxicity, usually a feeling of warmth, flushing, nausea, or increased salivation.

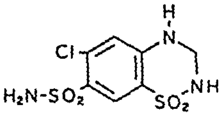
The initial orally given dose is 0.2 mg. In hospitalized patients, each subsequent dose is then increased by successive increments of 0.05 or 0.1 mg. until optimal hypotensive response is obtained or until side-effects become severe. This amount can then be given four times daily. If side-effects appear before the desired therapeutic effect is achieved, dosage should be reduced by 0.05 or 0.1 mg. and then again increased as the patient's tolerance permits.

In the ambulatory patient, dosage is increased more gradually. The initial dosage of 0.2 mg. four times daily is continued for one or two days. Then, if significant reduction in blood pressure has not occurred, the total daily dosage is increased by 0.2 to 0.4 mg. Similar increases may be made at intervals of 24 to 48 hours, until the desired effect has been achieved or until side-effects appear.

Preparations.—tablets 0.2 mg.

Year of introduction: 1958.
Pitman-Moore Company, Division of Allied Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of protoveratrine A.

Hydrochlorothiazide (Esidrix, HydroDiuril, Oretic).—6-Chloro-7-sulfamyl-2H-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxide.—The structural formula of hydrochlorothiazide may be represented as follows:



Actions and Uses.—Hydrochlorothiazide is a potent, orally effective diuretic agent, closely related to chlorothiazide, but effective in doses only one-tenth as great as those required for the latter drug. (See the monograph on chlorothiazide in J. A. M. A. 169:1191-1192 [March 14] 1959.)

Hydrochlorothiazide increases the urinary excretion of sodium and chloride and, to a lesser extent, that of potassium; fluid excretion is increased proportionately. Experimentally, hydrochlorothiazide has been shown to antagonize the sodium-retaining effect of aldosterone and desoxycorticosterone and the antidiuretic effect of vasopressin. In comparison with chlorothiazide, there is suggestive, but not conclusive, evidence that the maximal diuresis obtainable with hydrochlorothiazide may be slightly greater, that the ratio of sodium to potassium excretion may be somewhat higher, and that its diuretic effect may persist a little longer than that of the former drug.

Hydrochlorothiazide apparently produces its effects by inhibiting reabsorption of electrolytes by the renal tubules; it does not alter the renal blood flow or the glomerular filtration rate. In vitro, hydrochlorothiazide is considerably less active than chlorothiazide in inhibiting carbonic anhydrase; this action probably contributes only slightly, if at all, to the diuretic effect of usual doses in vivo. Hydrochlorothiazide ordinarily produces no appreciable change in serum electrolyte concentrations or in acid-base balance. Nevertheless, hypokalemia, hypochloremic alkalosis, and other electrolyte disturbances may be provoked by excessive doses or careless use of the drug.

Hydrochlorothiazide is well absorbed after oral administration. Its diuretic effect occurs promptly and becomes maximal within a few hours; some residual effect may persist for a total of 12 hours or more. The drug is eliminated largely by the kidney. Since its clearance greatly exceeds the glomerular filtration rate, it is assumed to be actively secreted by the renal tubules. There is no present evidence that metabolic degradation and storage play a significant part in the ultimate disposition of hydrochlorothiazide.

Hydrochlorothiazide does not differ significantly from chlorothiazide in its range of clinical application and, like the latter, is chiefly useful for the relief of edema and the adjunctive management of hypertension. It effectively induces diuresis and fluid loss in the presence of the edema of congestive heart failure, nephrosis, some forms of nephritis, toxemia of pregnancy, hepatic cirrhosis, and the fluid retention associated with premenstrual tension or therapy with corticotropin, corticosteroids, and some estrogens. There is no known contraindication to using it in conjunction with parenterally administered mercurials, with which its effects are additive.

In the management of hypertension, hydrochlorothiazide alone may occasionally produce a satisfactory reduction in blood pressure. It is most effective, however, when used concomitantly with reduced doses of other antihypertensive drugs, including ganglionic blocking agents, Rauwolfia alkaloids, Veratrum derivatives, and hydralazine.

Hydrochlorothiazide may be effective in patients who have become refractory to other diuretics, including chlorothiazide. Also, some patients in whom chlorothiazide produces prohibitive side-effects may tolerate hydrochlorothiazide.

Patients receiving hydrochlorothiazide should be carefully watched for signs of electrolyte depletion, such as weakness, lethargy, thirst, xerostomia, nausea, vomiting, muscle cramps, oliguria, and hypotension. Serum electrolyte determinations should be done periodically if the drug is given over a considerable period of time. Failure to correct early electrolyte disturbances may lead to convulsions, coma, and death.

Hydrochlorothiazide, like chlorothiazide, should be used with great caution in the presence of hepatic cirrhosis, marked renal impairment, and in patients receiving digitalis. The complications which may attend the use of hydrochlorothiazide in these conditions and the measures which should be employed to prevent or combat them are similar to those for chlorothiazide.

Other side-effects which have been observed with the use of hydrochlorothiazide include thrombocytopenic purpura, photosensitivity, skin eruption, and gastrointestinal disturbances.

Dosage.—Hydrochlorothiazide is administered orally. The dosage must be adjusted in accordance with the requirements and tolerance of the individual patient. The total daily dosage should not exceed 200 mg., as this appears to be the maximal therapeutic dosage, above which little or no additional activity seems to occur.

The doses usually required for initiating diuresis in the presence of edema range from 25 to 200 mg. per day. Smaller maintenance doses may be adequate to prevent recurrence of edema once excess fluid has been eliminated. In the adjunctive management of hypertension, 25 to 100 mg. per day is given, usually in conjunction with reduced doses of other hypotensive agents. The use of hydrochlorothiazide often makes possible some liberalization of the salt intake in both hypertension and conditions involving edema. For the relief of premenstrual tension, 25 to 50 mg. given once or twice daily may be tried.

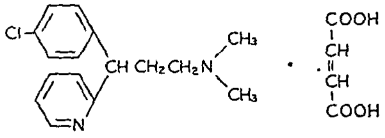
Administration of the drug early in the day will render the complication of nocturia less troublesome. Daily administration of 240 cc. (8 oz.) of tomato or citrus fruit juice will help to prevent potassium depletion and is indicated in patients in whom hypokalemia is particularly likely to occur or in whom it is especially to be feared. Potassium chloride, in doses of 2 to 6 Gm. daily, may be substituted for the fruit juice if desired.

Preparations.—tablets 25 mg. and 50 mg.

Year of introduction: 1959.

Ciba Pharmaceutical Products, Inc., and Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of hydrochlorothiazide.

Dexchlorpheniramine Maleate (Polaramine Maleate).—*d*-2-[*p*-Chloro-α-(2-dimethylaminoethyl) benzyl] pyridine maleate.—The structural formula of dexchlorpheniramine maleate may be represented as follows:



Actions and Uses.—Dexchlorpheniramine maleate is the dextrorotatory isomer of racemic chlorpheniramine maleate. Pharmacological studies with the dextro and levo isomers as well as the racemic mixture show that antihistaminic activity resides primarily in the dextrorotatory component. Thus, the *d*-isomer is about twice as potent as the racemate; the *l*-isomer has only about 1/100 the antihistaminic activity of the racemate. Since the toxicities of all three components are about the same, the fact that the same histamine-antagonizing effects may be achieved with doses of dexchlorpheniramine that are only half those required for chlorpheniramine would indicate a greater margin of safety for the *d*-isomer. Clinical observations have confirmed the high degree of effectiveness and low incidence of side-effects with dexchlorpheniramine. (See the general statement on histamine-antagonizing agents in New and Nonofficial Drugs.)

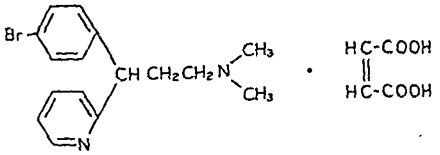
Dosage.—Dexchlorpheniramine is administered orally. For adults, the usual dose is 2 mg. three or four times daily. Alternatively, a single repeat action tablet containing a total of 4 or 6 mg. may be taken in the morning and again before retiring. These doses are reduced to one-half for children under 12 years of age and to one-fourth for infants.

Preparations.—syrup 0.4 mg. per cc.; tablets 2 mg.; tablets (repeat action) 4 mg. and 6 mg.

Year of introduction: 1958.

Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of dexchlorpheniramine maleate.

Dexbrompheniramine Maleate (Disomer).—*d*-2-[*p*-Bromo-α-(2-dimethylaminoethyl)benzyl] pyridine maleate.—The structural formula of dexbrompheniramine maleate may be represented as follows:



Actions and Uses.—Dexbrompheniramine maleate is the dextrorotatory isomer of brompheniramine maleate, the racemic mixture. Pharmacological studies have shown that the antihistaminic activity of the racemate resides almost exclusively in the *d*-isomer. On the other hand, there is little difference in the toxicities of either the *d*-isomer or *l*-isomer and the *d,l*-mixture in experimental animals. Thus, dexbrompheniramine is about twice as potent but no more toxic than brompheniramine. Clinically, the drug appears to be a highly effective antihistamine in very low doses. Side-effects, thus far limited to drowsiness, have occurred in less than one-tenth of the cases. Dexbrompheniramine, therefore, has a high therapeutic index. (See the general statement on histamine-antagonizing agents in New and Nonofficial Drugs.)

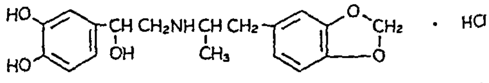
Dosage.—Dexbrompheniramine maleate is administered orally. The usual dose for adults is 2 mg. four times daily; in occasional patients, this dose may be doubled. For children, doses of 1 mg. are given four times a day. The dosage for infants is 0.5 mg. four times daily.

Preparations.—syrup, 0.4 mg. per cc.; tablets, 2 mg.; tablets (repeat action) 4 mg. and 6 mg.

Year of introduction: 1959.

White Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of dexbrompheniramine maleate.

Protokylol Hydrochloride (Caytine).—α[(α-Methyl-3,4-methylenedioxyphenethylamino)methyl] protocatechuyl alcohol hydrochloride.—The structural formula of protokylol hydrochloride may be represented as follows:



Actions and Uses.—Protokylol hydrochloride, a sympathomimetic amine, resembles isoproterenol hydrochloride in its pattern of pharmacological activity. Used principally as a bronchodilator, it may afford symptomatic relief of dyspnea and objective signs of improved respiratory function in such respiratory illnesses as bronchial asthma, chronic pulmonary emphysema, pulmonary fibrosis, chronic bronchitis, and bronchiectasis. In patients responding favorably, the drug produces a temporary increase in vital capacity, maximal breathing capacity, and expiratory velocity and a decrease in bronchial resistance. Although there is no evidence that it has any direct effect on the volume or character of respiratory secretion, its bronchodilating effect may facilitate expectoration of excessive secretion. When administered orally in the long-term management of chronic bronchial asthma, it seems to be about as effective as ephedrine. For the management of acute dyspneic episodes, it may be given by nebulization or injection and, when so used, produces results comparable to those of isoproterenol or epinephrine. Some patients who have become refractory to other bronchodilators remain responsive to protokylol hydrochloride; other patients, because of individual variation in response, may find it more helpful than other drugs.

Protokylol hydrochloride apparently is well absorbed after oral administration; effects are discernible within 30 to 90 minutes and persist for three to four hours. After inhalation of nebulized solutions or after intramuscular injection, effects appear within 5 to 10 minutes.

Side-Effects.—Like other adrenergic bronchodilators, in effective doses, protokylol hydrochloride not infrequently produces disagreeable side-effects, reflecting its action on the cardiovascular and central nervous systems. After usual oral doses, tachycardia occurs infrequently, whereas the blood pressure is not altered. On the other hand, larger oral doses or parenterally administered doses are quite often followed by tachycardia and palpitation; even in patients with quite severe tachycardia, however, the blood pressure ordinarily shows little change. Electrocardiographic studies have revealed no changes other than sinus tachycardia.

Other reported side-effects include tremulousness, tenseness, insomnia, dizziness, weakness, and nausea.

Experimental Pharmacology.—Protokylol hydrochloride is a potent inhibitor of smooth muscle, a powerful vasodepressor agent, and a cardiac stimulant. Intravenous injections in animals produce a sharp but fleeting fall in blood pressure, a decrease in total peripheral resistance, augmentation of the cardiac rate and output, increase in the respiratory rate, and a suppression of intestinal motility. Its bronchodilating activity is evident both in the intact animal and in isolated preparations; it is effective in relaxing bronchospasm induced either by histamine or by cholinergic agents and, in this respect, is approximately equal in potency to isoproterenol.

Dosage.—Protokylol hydrochloride is administered orally, by intramuscular or subcutaneous injection, or by inhalation.

For the long-term management of bronchial asthma and other chronic respiratory illnesses, 2 to 4 mg. is given orally four times daily, usually with or after meals (in order to minimize side-effects) and at bedtime. A barbiturate or other sedative may be given concomitantly, if necessary, to control apprehension, nervousness, and other symptoms of central nervous system stimulation.

In the management of subacute or acute exacerbations of bronchial asthma, 0.1 to 0.5 mg. of protokylol hydrochloride may be given by intramuscular or subcutaneous injection. This can be supplemented, if necessary, by inhalations of nebulized solutions four to six times daily. Dosage is adjusted, within the stated dosage range, in accordance with the severity of symptoms and the response of the patient.

Because of its potential ability to cause marked cardiac acceleration, protokylol hydrochloride is probably contraindicated in the presence of serious cardiac arrhythmias or insufficiency of the coronary circulation.

Preparations.—solution (inhalant) 1:100; solution (injection) 0.5 mg. in 1 cc.; tablets 2 mg.

Year of introduction: 1959.

Lakeside Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of protokylol hydrochloride.

VITAMIN K DEFICIENCY IN RATS FED IRRADIATED BEEF.—Evaluation of the nutritive value and appraisal of the toxicity of irradiated foods are imperative before this processing method is commercially applied. . . . Ground beef, irradiated at 2.79 and 5.58 million rad, and raw ground beef were supplied . . . in sealed cans by the Department of the Army. . . . Consumption of diets containing gamma-ray irradiated (2.79 or 5.58 $\times 10^6$ rad) beef resulted in internal hemorrhages and prolonged prothrombin times in growing male rats. Generally the female rat did not show this syndrome. The lesion was induced by freshly irradiated beef as well as irradiated beef which has been stored for over 6 months at room temperature. Supplementation with vitamin K prevented the hemorrhagic diathesis in rats consuming irradiated beef.—V. C. Metta, M. S. Mameesh, and B. C. Johnson, Vitamin K Deficiency in Rats Induced by the Feeding of Irradiated Beef, *The Journal of Nutrition*, September, 1959.

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PROTEIN SYNTHESIS

PROTEIN molecules are the basic units of the expression of form and function in living matter. Their many varieties—as structural components and as enzymes—determine the uniqueness of species and of individuals within species. Proteins are linear polymers made up of 20 repeating units (amino acids). Although naturally occurring proteins have a complex secondary and tertiary structure it is probable that this coiling and folding is a spontaneous result of the order and kind of amino acids in the primary chain. The over-all arbiter of the protein character of an individual organism is its genetic material—deoxyribonucleic acid (DNA). Passed down from generation to generation in the germ cells, these giant molecules maintain the genetic integrity of species. DNA molecules are linear polymers made up of four repeating units (nucleotides). An increasingly popular working hypothesis among molecular biologists, sometimes called "The Dogma," is that there may be a simple, determinative relationship between the linear structure of DNA and the linear structure of proteins: that unique sequences of nucleotides in DNA may determine unique sequences of amino acids in protein.

The "coding problem," to which the theoreticians in this field have applied themselves, is the problem of finding the code used by DNA to translate unambiguously its language of four symbols into the protein language of 20 symbols. The hypothesis is supported by three main kinds of evidence. First, experiments on bacterial transformation and bacteriophage infection suggest that DNA alone can transmit genetic information and that it therefore must contain all the information necessary to fabricate all the proteins of the organism. Second, studies on mutation and recombination in micro-organisms point to the probability that a mutation is an alteration of a very small segment of DNA—perhaps a change in a single nucleotide. Third, the mutation which results in sickle-cell anemia expresses itself as a substitution of a single amino acid in the protein hemoglobin. Intensive research is now under way to find other examples of the hemoglobin case by exploring systems in which the effect of mutation on primary protein structure may be more conveniently studied. Micro-organisms offer the most promising area because of their short generation time, their relative simplicity, and the controllability of their genetics.

The foregoing approaches do not generally ask questions about intermediate steps. Another of the flourishing areas of biochemical research today is the study of the chemical events on the path of protein synthesis. Most of our information in this area has come from a study of mammalian cell-free preparations in which are isotopically labeled amino acids. A number of important developments have occurred in the past five years.

We now know that amino acids, before being able to condense with one another to form protein, must first be brought into a reactive state, or activated. Cellular energy in the form of metabolically generated adenosine triphosphate (ATP) must be funneled into the process. It now appears that this is accomplished by 20 amino acid–activating enzymes, each one specific for one of the 20 amino acids. Each of these enzymes brings its specific amino acid and ATP together to form a new compound, aminoacyl adenylate (or adenosine monophosphate-amino acid) in which the carboxyl group of the amino acid reacts with the innermost phosphate of ATP in such a way as to usurp the place of the two terminal phosphates of ATP. These compounds are the biologically activated states of the amino acids and remain firmly bound to the activating enzymes until used for subsequent steps in protein synthesis.

The next step in the process has been unearthed only in the last three years and sheds direct light on the role of nucleic acids in protein synthesis. Each amino acid–activating enzyme attaches its specific activated amino acid to the end of a small ribonucleic acid (RNA) molecule called transfer RNA or soluble RNA. The nature of the chemical bond between amino acid and RNA is such that the amino acid remains in the activated state. Each transfer RNA molecule will bind one, and only one, amino acid. Since RNA, like DNA, is a polymer composed of four repeating nucleotide units, its seems inescapable, although it has not yet been proved, that a particular ordering of the nucleotides in the transfer RNA molecules underlines their specificity of reaction with amino acids. Thus, a key to the coding problem may lie in this group of reactions.

The foregoing events occur in the soluble phase of the cell cytoplasm. The actual final construction of protein molecules occurs in small cytoplasmic particles called ribosomes. These particles are so named because they contain most of the cell's ribonucleic acid (exclusive, of course, of transfer RNA and of a small amount of nuclear RNA). This RNA differs from the transfer RNA in being of much higher molecular weight, and apparently arranged in space as a definite, recognizable cellular structure. These structures are remarkably like viruses in many respects.

Current investigations show that the transfer RNA molecules bring the attached activated amino acids to this ribosome assembly line where the amino acids are then linked together in peptide bonds to form new protein. Transfer RNA therefore acts as a shuttle, transferring activated amino acids from activating enzymes to ribosomes.

There is reason to believe that the ribosome RNA is a template for synthesis of protein (it is currently being called "template RNA")—that it is coded to arrange the amino acids on its surface in the proper order prior to their condensation to form protein. The current working hypothesis is that transfer RNA confers "recognizability" on each amino acid so that the template may put it in its proper place. This could be brought about by the known highly specific chemical interactions between RNA molecules—the nucleotides of the transfer RNA binding specifically to complementary nucleotides on the template, thereby properly locating the amino acid. Experimental attempts to prove or disprove this hypothesis are now under way.

If the RNA of the ribosomes is a template for arranging the amino acids, it must receive its genetic sequence information from the DNA of the nucleus. This could most simply be accomplished by a direct synthesis of ribosome RNA from DNA in the nucleus in a manner identical to the duplication of DNA itself. Although this is chemically plausible and preliminary experimentation suggests that cytoplasmic RNA originates in the nucleus, this work is in its early phases. If such proves to be the case, the steps from DNA to protein would have been broadly defined and the secrets of the code susceptible to direct attack.

The delineation of these synthetic steps is a necessary preliminary to the exploration of control mechanisms in cells—the control growth and in higher organisms of differentiation. Logical chemical approaches to the treatment of aberrations of growth may then become feasible. The role of the ribosomes as the cells' chief protein builders takes on heightened significance in light of their chemical similarity to viruses and the possible part played by the latter in cancer.

ASCLEPIUS—MAN OR MYTH

Asclepius, Asclepios, Asklepios, Aesculapius (Latin), or Ασκληπιος (Greek), if one has a yearning for the good old days of resinated wine and chariot races, is probably the most venerated physician of all times. Scholia in Homer's Iliad suggests that the name Asklepios was derived from words meaning applying (askein) and making the limbs gentle (epia). Another interpretation ascribes his name to "healing soothingly and for deferring the withering that comes with death." Yet a third writer affirms that Asklepios was originally known as Epios because of his gentleness and calmness. After he had cured Askles, the tyrant of Epidaurus who suffered from ophthalmia, he was called Asklepios, with the accent on the penult. Demosthenes changed the pronunciation by accenting the antepenult. Asclepius is to be distinguished from Asclepiad, a generic appellation for a priest of the temple of Asclepius, from Asclepias, a genus of Asclepiadaceous plants, and from Asclepiades, a Bithynian physician of the second century, B. C., who practiced in Rome and openly admitted opposition to the teachings of Hippocrates.

The fact or fancy, man or myth, physical being or deity of Asclepius probably never will be resolved. The evidence in support of a practicing physician skilled in the art and widely recognized throughout ancient Greece, and even as distant as Egypt, is impressive to the present-day traveler. Because of his clinical acumen and his skill in combating morbidity as well as mortality, the ancient writers described him as being with a serpent. The sculptor who carved for eternity and the painter who used oils and pigments for a shorter period of time gave him a serpent, with the implication that those who avail themselves of medical science undergo a biological change making them similar to the serpent; patients are young again after illness and are able to slough off old age. Also the serpent is a sign of attention, much of which is required in medical treatment. The staff around which the serpent twines is a symbol of support. "It prevents our falling into sickness and although stumbling without the staff we would fall even sooner than need be."

Whence came Asclepius? This question is answered in the legend of the son of Apollo and Coronis. "In all Thessaly there was no fairer maid

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Edelstein, E. J., and Edelstein, L.: Asclepius: Collection and Interpretation of Testimonies, Baltimore, Johns Hopkins Press, 1945.

than Coronis of Larissa. She surely found favor in thy eyes, O Delphic god, so long as she was chaste —or undetected. But the bird of Thoebus discovered her unchastity and told his master that he had seen Coronis lying beside the youth of Thessaly." Asclepius was the offspring of this union. In maturity he excelled in nature and keenness of mind; he strove after medical knowledge and discovered many of the things that tend to promote health. He advanced so far in reputation as to cure many of the sick who had been despaired of, contrary to all expectations. "He revived some who had died." The story was current that even Pluto, bringing a charge against Asclepius, accused him before Zeus on the ground that the scope of his power was diminishing, for the dead were continually growing fewer because they were healed by Asclepius.

The Homeric Asclepius is said to have restored life to Glaucus, the son of Minos, on the island of Crete. It is on this island that the best preserved ruins of Minoan civilization are extant today. This golden era of pre-Hellenic Greece was in flower from 3400 to 1200 B. C. The most famous antiquities on the island are the partially restored palace of King Minos at Knossos and the excavation at Phaistos. Nearby is the court from which Daedalus took off in his flying machine. Asclepius practiced medicine also at Delphi, the site of the most famous oracle of Greece. An impressive portion of this oracle remains on the side of the hill near Mount Parnassus. The two greatest Asclepian temples that the traveler may see on the tourist trails are fabulous in extent and remarkable in their state of preservation. On the island of Cos, the Sacred Spring is still flowing in the Asclepian Temple. At Epidaurus, on the Peloponnesus, south of Athens, a remarkably well preserved amphitheater is only a few steps from the Asclepian Temple.

Like many modern physicians, the first Asclepius bore at least four children. His daughters were Hygeia and Panacea. Two sons, Podalirius and Machaon, became physicians. Because of their professional skill they were called into military service in the Trojan War under Agamemnon. It was an ideal combination of internal medicine and surgery. "Podalirius treated diseases by diet while his brother Machaon, having been blessed with more agile hands, practiced surgery only." It is stated that King Agamemnon summoned Machaon to cure the wounded Menelaus. Although Schliemann, the unorthodox German archeologist, was proved wrong in his assumption that he had discovered the tomb of Agamemnon, the bathroom in the palace where Orestes slew his father is pointed out to the modern traveler. Also, the beehive tombs, huge vaulted underground chambers, may be seen on a neighboring hill. Undoubtedly Agamemnon was buried in a similar tomb nearby.

Hippocrates was the 18th descendant of Asclepius through Podalirius. If Hippocrates was a man of flesh and blood, could not Asclepius seven centuries earlier likewise have been a man and not a myth?

PERSON TO PERSON

Physicians comprise a coterie of profession personnel who have latent or overt talent in con position that they cannot for long escape. The c pacity for expression of recurring thoughts in som instances is well recognized by their bibulous bret ren and may even reach the written stage. In othe the urge is present but lies dormant. Whether o is a little-known William B. Bean or a poor ma Walter Lippmann, this appeal is applicable. "Le ters to the Editor" is the pertinent problem. Th physician need not wear a toga to be heard on th forum. One does not need even a discarded box Procter and Gamble's best.

The preparation of a patient's history in medic school, a summary report as an intern, or an ess on interesting cases as a dissertation before a me ical society provides an opportunity for writt expression. Such a background may suffice to sta the physician on his journalistic course. A letter the editor provides one medium for expressio Once the journey is under way, there should l considerable satisfaction in the discovery that t editor to whom the letter is addressed recogniz merit in the composition. Seriousness is demande in many instances, and even a taint of flippan would be a demonstration of poor taste. In oth instances, a small portion of the lingual apparatu approximating the buccal mucosa, would not l inappropriate. At least the editor in charge of th bureau has been instructed to be lenient if a leave ing touch is detected. Nor will there be automat editing in order to conform to a voluminous boo of "precedent in composition." Expression from th soul may be an example of an instructive exercis similar to the painful preparation of a scientif manuscript, sentence by sentence. This will l respected. Furthermore, praise, flattery, even wa ranted criticism will be accepted in rotation. Prais without exuberance, flattery without insincerit and criticism without rancor are considered a ceptable attributes of expression. This editorial to be interpreted as a bare-faced attempt at solic tation of letters. However, do not assume that th Dillon mission to Europe is an adult Wester televised from the Continent.

ORGANIZATION SECTION

STATEMENT TO SENATE WAYS AND MEANS COMMITTEE

Nov. 13, 1959

The Honorable Wilbur D. Mills, Chairman
Committee on Ways and Means
U. S. House of Representatives
New House Office Building
Washington 25, D. C.

Dear Chairman Mills:

The American Medical Association has been advised that the Ways and Means Committee has scheduled hearings next week concerning a possible general revision of the Internal Revenue Code. Inasmuch as our Association is interested in a number of the subjects in this field which you are going to discuss, I am submitting this statement with the request that it be included in the printed record of the hearings.

We readily appreciate the scope of the task which you have undertaken. In our opinion, some of the revisions of the Code which have been adopted in the past have created more inequities than they have remedied and have so complicated our system of income taxation that a reexamination of basic concepts is essential to a general revision of the Code. We are in accord with the premise which you have stated as to the need for protecting and broadening the tax base so as to permit a reduction in tax rates without necessarily impairing total revenue to the government.

We believe that graduated income tax rates which reach confiscatory levels are especially unfair to professional persons and others who derive their income from services which they personally perform. Special treatment for the taxation of capital gains and different types of credits, deductions, and allowances have tended to soften the effect of graduated taxes with reference to income earned from sources other than the rendition of personal services. Business conducted through corporations also provides opportunities for minimizing the effects of higher personal tax rates. We believe that a simplification of our system of taxation, to permit lower rates for all, is seriously needed.

It is our opinion that the major difficulties in the tax structure stem from the inequities and exceptions which have been compounded with reference to the taxation of income as such. Business transactions are governed more by tax considerations than they are by the normal economics of the market place. We do not believe that these abnormal factors should be confused with the considerations which make it socially desirable to provide personal (rather than business) tax relief for the aged, the disabled, and those for whom illness has required unusual expenditures for medical care.

There are, as you know, legislative proposals now pending before your Committee which would, if enacted, provide federally financed medical and hospital care for Social Security beneficiaries. To the extent that the health care problems of the aged are economic in nature, we believe that a partial solution may be provided through a more liberal tax deduction program for persons over the age of 65 years. Such a program would facilitate the provision of health care on an individually financed basis without the dangers implicit in the adoption of a federal system of hospitalization and medical care.

We also wish to reaffirm our position that physicians, dentists, farmers, lawyers, architects, veterinarians, merchants, and many others of the nation's self-employed have long been neglected in federal tax legislation relating to pensions. With high taxes and inflated living costs, it is difficult for persons in these occupations to set aside adequate funds for retirement without a tax deferment similar to that available to corporate employees. The favorable action taken by your Committee and the House of Representatives on H. R. 10, 86th Congress, earlier this year is appreciated by all of the self-employed.

With respect to tax-exempt organizations, which we note will be the subject of a panel discussion on Dec. 15, it is our opinion that the contributions made to society by professional and trade organizations justify a more liberal attitude with respect to them from the standpoint of tax exemption. In considering this subject, we believe that the contributions which they are making should not be impeded merely to provide the means for dealing with isolated abuses.

If we can be of service to your Committee in any way, either in expressing our opinions on proposed revisions in the tax law or in supplying information, you may be assured of our willingness to cooperate.

Very truly yours,
F. J. L. Blasingame, M.D.
Executive Vice-President

MEDICAL NEWS

CALIFORNIA

Course in Dermatology for Pharmacists.—The University of California School of Pharmacy Department of Continuing Medical Education, San Francisco, will present, "Dermatology for Pharmacists" Jan. 21 & 22 as a series of lectures and demonstrations pertaining to dermatologic therapy. Program chairmen will be Donald C. Brodie, Ph.D., professor of pharmacology, and Dr. S. William Levy, associate clinical professor of dermatology. Eleven topics are scheduled. A panel discussion, "Sunburn, Prevention and Treatment" will be conducted the morning of Jan. 22. Louis C. Zopf, Sc.D. dean of the College of Pharmacology, State University of Iowa, will present "Facts and Pharmacy's Future," at the dinner the evening of Jan. 21. Registration fee is $30. For information, write Dr. Seymour M. Farber, University of California Medical Center, San Francisco 22.

CONNECTICUT

Appoint Deputy Health Commissioners.—Appointment of three deputy commissioners in order to effect reorganization and expansion of the Connecticut state health program authorized last spring by the Connecticut General Assembly were announced by Dr. Franklin M. Foote, commissioner of health. Dr. Harold S. Barrett, Hartford, was named deputy commissioner of the Office of Public Health which includes five major divisions: community health services, medical services, preventable diseases, sanitary engineering, and laboratory services. Dr. Paul S. Phelps, Hartford, is deputy commissioner for the Office of Tuberculosis Control, Hospital Care and Rehabilitation, administering four chronic disease hospitals with 1,000 beds, and 15 field clinics. Mr. Bert W. Schmickel, former superintendent of the Southbury Training School, was appointed acting deputy commissioner for the Office of Mental Retardation and will have administrative responsibility for the two state training schools with 3,700 retardates, and for community programs including diagnostic centers, day-care facilities, and rehabilitation services. Completion of the state health reorganization was announced effective Dec. 15, by Governor Abraham Ribicoff.

FLORIDA

Seminar in Miami Beach.—A seminar in obstetrics and gynecology will be held at St. Francis Hospital, Miami Beach, Feb. 4-6, from 9 a. m. until noon. The seminar will be under the professorship of Dr. Herbert E. Schmitz, professor of obstetrics and gynecology at the Stritch School of Medicine of Loyola University, Chicago. The program is as follows:

Feb. 4.—Benign and Malignant Lesions of the Vulva. Pre and Invasive Carcinoma of the Cervix.
Feb. 5.—Endometrial Carcinoma. Film on Ovarian Tumors, with a Discussion of the Treatment Including Chemotherapy.
Feb. 6.—Indications for Hysterectomy. Diagnosis and Treatment of Endometrium. Treatment of Carcinoma of the Cervix Complicating Pregnancy.

For information, write Dr. John A. Heffernan, 1549 N. E. 123rd St., North Miami, Fla.

LOUISIANA

Exhibit Wins Gold Award.—An exhibit, "Electron Microscope Studies of the Human Epidermis," presenting original research work done in the departments of pathology and anatomy of Tulane University School of Medicine, New Orleans, was given the Gold Award at the meeting of the American Academy of Dermatology and Syphilology in Chicago, Dec. 10. The exhibit was prepared and presented by Dr. Wallace H. Clark Jr., associate professor of pathology, Richard G. Hibbs, Ph.D., assistant professor of anatomy, and Mrs. Mildred C. Watson, research associate in pathology. The exhibit demonstrated that the melanocyte is an anatomically distinctive unit within the epidermis distinguishable from ordinary epidermal cells and the "intercellular bridge" was shown to be a complex attachment zone between cells and not fibrils coursing from one cell to another.

MICHIGAN

Conference of Health Directors.—The 1960 state health commissioner's conference of local health directors will be held at the Michigan Department of Health in Lansing on Feb. 3-4. The conference will be the 10th called by Dr. Albert E. Heustis since he became state health commissioner in 1948. At each conference, public health topics of special interest to Michigan's 43 full-time local health departments as well as the state health department are discussed. The 43 local departments serve about 90% of the state's population. The four main topics selected for discussion at the February meeting are

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

as follows: nursing home licensing, home nursing care, local health department duties in civil defense, and detecting disease by group testing. Chairman of the committee of local health officers working with Dr. Heustis and his staff in planning the conference is Dr. Ervin J. Brenner, Mount Pleasant, director of the Central Michigan District Health Department, serving Isabella, Mecosta, and Osceola counties.

MONTANA

Big Mountain Medical Meeting.—The Flathead County Medical Society will present a Big Mountain Medical Meeting in Whitefish Jan. 20-30. The following are listed as program speakers: Drs. Dale H. Correa, Cabot Wohlrabe, Richard C. Gaard, Stuart Lane Arey, Elizabeth K. B. Jerome, Richard C. Tucker, John H. Linner, John P. Wendland, Graham G. Smith, Arnold J. Kremen, George Tangen, and Carl O. Rice, of Minneapolis, Minn. A movie, "Intraocular Foreign Bodies," will be presented by Dr. Wendland the afternoon of Jan. 29, and a dinner is planned for that evening. For information, write Dr. George H. Gould, Sunset Boulevard and Nevada Street, Kalispell, Mont., Chairman.

NEW YORK

Faculty Appointments.—Three Schenectady physicians were named to the faculty in the department of obstetrics and gynecology at Albany Medical College, Harold C. Wiggers, Ph.D., dean of the college, announced. They are Dr. William J. Jameson, Dr. Kurt H. Meyerhoff, and Dr. Louis P. Tischler. Dr. Jameson was appointed an assistant clinical professor, and Drs. Meyerhoff and Tischler have been named instructors. The three doctors will devote part-time to teaching and will continue their private practices in Schenectady.

New York City

Dr. Gitlin to Give Lecture.—Dr. David Gitlin, of Harvard University Medical School, Boston, will give a William Hinz Memorial Lecture, "Humoral and Genetic Factors in Infection," before the Bronx Pediatric Society on Wednesday, March 9, 8:30 p. m., in the auditorium of Morrisania Hospital in the Bronx.

Dr. Masterson Receives Catholic Physician Award.—Dr. John J. Masterson, of Brooklyn, was presented with the Catholic Physician of the Year award by the National Federation of Catholic Physicians Guilds in Dallas, Texas. Dr. Masterson served as president of the NFCPG from 1942 to 1947. He began specializing in radiology in 1908. The Brooklyn physician has been the New York State delegate of the American Medical Association for the last 25 years.

OKLAHOMA

Meeting on General Practice in Tulsa.—Various fields of medicine and surgery will provide topics for the speakers for the 12th annual meeting of the Oklahoma Chapter of the American Academy of General Practice to be held in Tulsa, Feb. 15-16. Site of the two-day meeting will be the Tulsa Hotel. Seven guest speakers are listed: Drs. Elwood K. Hammond, Louisville, Ky.; Benjamin Felson, Cincinnati; James W. Kelley, Tulsa; Isadore Dyer, New Orleans; Carlo Scuderi, Chicago; Anthony S. Ridolfo, Indianapolis; and William D. Snively Jr., Evansville, Ind. Dr. Marshall O. Hart, Tulsa, is general chairman for the 1960 meeting.

Dr. Heatley Honored.—The Alumni Association of the University of Oklahoma School of Medicine honored Dr. John E. Heatley, Oklahoma City, as "Professor Emeritus of the Year" during the annual banquet meeting Oct. 25 at Oklahoma City. Dr. John R. Taylor, Kingfisher, former president-elect was installed as association president, succeeding Dr. Carl H. Bailey, Stroud. Dr. Heatley, a former chairman of the department of radiology, was appointed professor emeritus of diagnostic radiology in 1949. A "Professor Emeritus" plaque also was presented Dr. Wann Langston, Oklahoma City, professor emeritus of medicine, who was cited in 1957. The practice of presenting plaques to the honorees was not started until last year, and Dr. Langston was in Europe when the presentation to past-honorees was made at the 1958 session.

PENNSYLVANIA

Laboratory for Rheumatologic and Orthopedic Research.—The University of Pittsburgh School of Medicine received a $78,768 grant from the National Institutes of Health to help construct and equip a Laboratory for Rheumatologic and Orthopedic Research. This amount will be matched by university funds to provide a total of nearly $160.-000 for the project. The funds will be used to purchase additional equipment and to complete interior construction on the ninth floor of the existing wing between the Schools of the Health Professions building and Presbyterian Hospital. Construction is scheduled to start this spring. Research in the laboratory will be under the joint supervision of Dr. Albert B. Ferguson Jr., professor of orthopedic surgery, and Dr. Gerald P. Rodnan, assistant professor of medicine. The new area will more than double the amount of space currently devoted to rheumatologic and orthopedic research at the university. The joint laboratory will include facilities for pathology, chemistry, physiology, serology, x-rays, and radioisotopes; an operating room for experimental surgery; animal quarters; and office space.

Philadelphia

Annual Oration.—Dr. Lawson Wilkins, professor of pediatrics, Johns Hopkins University School of Medicine, Baltimore, was guest speaker at the annual B. A. Thomas Oration of the Philadelphia Urological Society Jan. 11. His topic was "Abnormalities of Sex Differentiation: Etiology, Diagnosis, Selection of Sex Treatment."

Personal.—Dr. Valy Menkin, guest investigator at the Henry Phipps Institute of the University of Pennsylvania, returned from Europe after having been sent as an exchange visiting professor to France. Lectures were delivered in France, Holland, and in Belgium. The Institute Pasteur in Paris and the University of Liege, Belgium, each awarded a medal to Professor Menkin.——Dr. Joseph Seifter was appointed director of basic medical sciences research for Wyeth Laboratories. Dr. Seifter, associated with the pharmaceutical company since 1944, was a member of the medical school faculty at Western Reserve University, Cleveland, for several years before joining Wyeth.

Intern Awarded Prize in Preventive Medicine.—The first William Harvey Perkins Prize in Preventive Medicine of the College of Physicians of Philadelphia was awarded to Dr. Cyril F. Conway Jr., at a meeting of the Section on Public Health, Preventive and Industrial Medicine Oct. 13. Dr. Conway, a graduate of Temple University School of Medicine in 1959, is interning at Nazareth Hospital. The prize, a certificate and $100, was presented to Dr. Conway by Dr. Perkins on behalf of the section. The prize essay, "Tranquilizers—Their Use and Abuse," was judged best among entries submitted by students enrolled in Philadelphia medical schools during the past year. Dr. Perkins, who recently retired as professor of preventive medicine and department head at Jefferson, also served as dean of his alma mater from 1941 to 1950. The student essay contest was inaugurated in his honor last year.

Grant Supports Cardiovascular Research in Animals.—A $1,100,000 ten-year grant for research in the comparative diseases of the heart and blood vessels of animals and man at the University of Pennsylvania became effective Jan. 1. David K. Detweiler, D.V.M., associate professor of veterinary pharmacology, and chief of the laboratory of physiology and pharmacology at the University of Pennsylvania School of Veterinary Medicine, will serve as director and principal investigator of the research effort, supported by the largest research grant ever made to a School of Veterinary Medicine by the U. S. Public Health Service. The financial support, in the form of an original grant of $110,000, for 1960, from the National Heart Institute, represents an expansion of that institute's program in veterinary research, and will be accompanied by a commitment which will provide the same amount for nine additional years. Dr. Detweiler will establish the University of Pennsylvania Comparative Cardiovascular Studies Unit, which will serve as a research center for the study of the comparative aspects of the cardiovascular systems of animals representing as many species as possible. The unit, which will also carry out an international training program for research in comparative cardiology of the *World Health Organization*, will be located in a now vacant building adjacent to the School of Veterinary Medicine's West Philadelphia campus. The research will be carried out in cooperation with other units of the university's Medical Division, including departments of the School of Veterinary Medicine, the School of Medicine, including the Robinette Foundation for Cardiovascular Research, and the Graduate School of Medicine. Also cooperating will be the university's Graduate School of Arts and Sciences, and the Penrose Research Laboratory of the Zoological Society of Philadelphia.

PUERTO RICO

Programs for Public Health.—Puerto Rico is launching an attack on heart disease, cancer, and other diseases which have become primary medical problems. The effectiveness of the commonwealth's public health program so far is reflected in its low death rate, 7 per 1,000 inhabitants, and in its lengthened average life span: over 68 years now as against 46 in 1940. In preparation for its new public health drive in the 1960's, the commonwealth in 1959 worked on a number of programs of which three are of particular significance:

(1) Construction began on a $55,000,000 medical center in San Juan. The first unit, a 150-bed cancer hospital, is scheduled to open in 1960. Other units, to be opened within six years, are a 450-bed general hospital, a 600-bed municipal hospital, an industrial hospital, a nursing home, and a physical rehabilitation center. Also planned is a School of Nursing which will complement the School of Medicine of the University of Puerto Rico. The center is being built under the Hill-Burton Act.

(2) In cooperation with the Atomic Energy Commission, development of the Puerto Rico Nuclear Center continued. Operated for AEC by the University of Puerto Rico, the Nuclear Center has facilities in being and under construction both in San Juan and at the university's Mayaguez campus on the west coast. The Dr. I. Gonzalez Martinez Oncological Hospital in San Juan houses the Radiotherapy and Cancer Division. There an 8,000-curie radiotherapy unit went into operation in 1959. At Mayaguez, headquarters for the Nuclear Center, a 10-kilowatt training reactor has been operating during the past few months, and a 1,000-kilowatt pool-type reactor is under construction and will go into operation in 1960. It will produce isotopes for medical and other types of research. The center is serving as a school of nuclear science and technology for students from Puerto Rico and Latin America as a whole.

(3) Outside the major metropolitan areas, a new program to establish well-rounded hospital and other public

health services in every municipality is under way. Thirty-three regional centers are in operation and the new program will about double that number in the next few years.

GENERAL

Society for Tropical Dermatology.—The International Society for Tropical Dermatology will hold its organizational meeting on Jan. 25, 8:00 p. m., at the New York Academy of Medicine, New York City. This meeting will include adoption of the constitution and bylaws, and the election of officers. All charter members are invited. For information, write Dr. Frederick S. Reiss, 870 Fifth Ave., New York 21, Organizing General Secretary.

Award for Medical Photography.—The Combined Colleges Bronze Medal, donated by the Royal College of Surgeons of England, the Royal College of Physicians of London, and the Royal College of Obstetricians and Gynaecologists, will again be awarded in 1960 to any person of any nationality whether a member of the Royal Photographic Society or not "for outstanding example of photography in the service of Medicine and Surgery." Work submitted or nominations for the award should be received by the Hon. Sec. of the Group, 16 Prince's Gate, London, S. W. 7, by Sept. 30.

Medical Seminar Cruise.—The Albany (N. Y.) Medical College of Union University will present its second annual shipboard postgraduate medical seminar aboard the S. S. Hanseatic, departing New York for Caribbean ports on March 29. The 14-day seminar-cruise will include stops at Curaçao, Cristobal, Kingston, and Port-au-Prince. The postgraduate program will consist of selected topics in internal medicine, pediatrics, surgery, and obstetrics and gynecology. Clinical pathological conferences will be included. The program constitutes 22 hours of category I credit toward the postgraduate requirements of the American Academy of General Practice. Details can be obtained by writing the Director of Postgraduate Education, The Albany Medical College of Union University, Albany 8, N. Y.

Clinical Meeting in Dallas.—The 29th annual spring clinical conference of the Dallas Southern Clinical Society will be held March 21-23 at the Statler Hilton Hotel, Dallas. The program will feature general assemblies, round-table luncheons, postgraduate lectures, panel discussions, a clinical pathological conference, technical exhibits, and a dinner dance. The following physicians are listed as guest speakers:

Drs. Douglas N. Buchanan and Edward L. Compere, Chicago; Robert E. Cooke, Baltimore; George Crile Jr., Cleveland; Arthur G. Devoe, Herman Elwyn, Milton Helpern, Lawrence S. Kubie, and Charles F. Wilkinson, New York City; William Dock, Brooklyn; James E. Eckenhoff and S. Leon Israel, Philadelphia; Benjamin Felson, Cincinnati; Aram Glorig Jr. and Daniel G. Morton, Los Angeles; Frank Hinman Jr., San Francisco; Charles G. Johnston, Detroit; and Robert E. Votaw, St. Louis.

Registration fee is $25. For information, write the Dallas Southern Clinical Society, Medical Arts Bldg., Dallas 1, Texas.

Program for Training in Neurological Disorders.—A special traineeship program was announced by the National Institute of Neurological Diseases and Blindness. The program offers an opportunity to qualified basic scientists and clinicians for advanced study and research training in neurological and sensory disorders, in the U. S. A. or abroad. To qualify, candidates must have an M.D., Ph.D., or equivalent degree; three years or more of postdoctoral training or experience pertinent to the training desired; and American citizenship or declaration of intent filed. Given for periods of not less than 9 months and not more than 12, all awards are subject to renewal up to a total of 60 months. Stipends will be determined individually, and may range from $6,500 to $17,500 a year. Application may be made at any time. Information and forms may be obtained from Chief of Extramural Programs, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda 14, Md.

Prizes for Surgical Investigations.—Two prizes of $300 each are being offered in 1960 "for the most meritorious investigation in some phase of surgery or in the allied specialties of surgery" by the Woman's Auxiliary of the United States Section, International College of Surgeons. The investigations may also be in the fundamental sciences, provided the work has a definite bearing on some accredited surgical problem. Competition is open to graduates of medical schools who completed their internship or a year of residency within a period of five years prior to Jan. 1, 1960, excluding their terms of service in the armed forces. Manuscripts must be submitted to Dr. Horace E. Turner, chairman of the scholarship committee, U. S. Section, International College of Surgeons, 1516 Lake Shore Dr., Chicago 10, not later than July 1. The manuscripts of the prize papers will become the property of the college. Prize winners must present their papers at a meeting of the college. If no paper submitted is deemed worthy of the prize, the award may be withheld. Inquiries should be addressed to Dr. Turner.

Annual Meeting on Clinical Research.—The 13th annual meeting of the Western Society for Clinical Research will be held Jan. 28-30 at the Golden Bough Theater, Carmel, Calif. Dr. Arthur J. Seaman, Portland, Ore., will open the meeting with the president's address and will preside at the first session. The program includes 36 papers, the following of which will be introduced by members:

- The Rhesus Macaque as a Model of the Effects of Human Pregnancy on Iodine Metabolism, Dr. James T. Dowling, Newton, Mass., and Dr. Donald L. Hutchinson, Los Angeles.
- Increased Sensitivity of the Respiratory Center During Human Pregnancy, Drs. Donald M. Pitcairn and Robert D. Michel, Portland, Ore.
- The Effect of Temperature on the Viscosity of Sickle Cell Blood, Dr. Edward Rubenstein, San Mateo, Calif.
- A Method for Measuring "Effective Erythropoiesis," Dr. Arthur J. Samuels, Beverly Hills, Calif.
- The Chemical Substructure of Hemoglobin H; A Unique Type of Hemoglobin Molecule, Dr. Richard T. Jones and Walter A. Schroeder, Ph.D., Pasadena, Calif.

For information, write Dr. William N. Valentine, University of California Medical Center, Department of Medicine, Los Angeles 24, Calif., Secretary-Treasurer.

Doctoral Dissertations Available on Microfilm.—A plan for publishing a Doctoral Dissertation series was begun in 1938 by University Microfilms, Inc., of Ann Arbor, Mich. The plan operates as follows: The author of a dissertation writes a 600-word summary of his study and forwards it through his institution to University Microfilms along with his complete typescript dissertation. The summary is printed in "Dissertation Abstracts" while the complete manuscript is microfilmed and the master film copy is deposited in UM vaults for later duplication. About 6,000 dissertations in all fields are abstracted annually in the 98 institutions now cooperating in the plan. Complete dissertations may be ordered as microfilm or as enlargements. The annual subscription fee for "Dissertation Abstracts" is $20 for domestic subscribers, $22 for foreign. An index to all doctoral dissertations accepted by institutions of higher learning in the U. S. and Canada is also available. Both publications are sponsored by the Association of Research Libraries. For information, write University Microfilms, Inc., 313 N. First St., Ann Arbor, Mich.; or University Microfilms, Ltd., 44 Great Queen St., London, W. C. 2, England.

Meeting of Western Physicians.—The fifth annual meeting of the Western Association of Physicians will be held in Carmel, Calif. Jan 27-29. To open the meeting, Dr. David A. Rytand, Palo Alto, Calif., will present the president's address. Of the 14 papers scheduled for presentation at the two scientific sessions, the following will include invited authors:

- Biochemical Factors Affecting Liver Metabolism, A. Baird Hastings, Ph.D., La Jolla, Calif.
- Effects of Isoproterenol on Carbohydrate Metabolism of the Isolated Canine Heart, Drs. Loren C. Winterscheid, Robert A. Bruce, Jack B. Blumberg Robert M. Leyse, and K. Alvin Merendino, Seattle.
- Medical Experiences in Peru, Drs. Herbert N. Hultgren, San Francisco, and Warren B. Spickard, Seattle.
- The Prognosis of Conservatively Treated Essential Hypertension, Drs. Maurice Sokolow, San Francisco, and Dorothee Perloff, Sausalito, Calif.
- Factors Influencing Cardiac Output in Man, Dr. James V. Warren, Galveston, Texas.
- Atrophic Gastritis Experimentally Induced by a Preparation of Human Gastric Juice, Dr. Stewart G. Wolf Jr., Oklahoma City.
- Granulocyte Physiology in Normal Subjects, Drs. John W. Athens, Helen Ashenbrucker, George E. Cartwright, and Maxwell M. Wintrobe, Salt Lake City.
- The Mild Hemophilias, Drs. Paul M. Aggeler and M. Silvija Hoag, San Francisco.
- Use of Methemoglobin Reduction to Detect Abnormalities in Red Cell Carbohydrate Metabolism, Drs. Ernest R. Simon, Dr. David D. Kliewer, Emily R. Thompson, and Dr. Clement A. Finch, Seattle.

A business meeting will be held the afternoon of Jan. 29. For information, write Dr. Wade Volwiler, Department of Medicine, University of Washington, Seattle 5.

Travel Fellowship in Medical Education.—The China Medical Board of New York, Inc., recently decided to support an Alan Gregg Travel Fellowship in Medical Education to be awarded to a member of the faculty of an American medical school. The award, in memory of Alan Gregg, medical educator who died in June, 1956, will be awarded annually beginning in 1960. It is to enable a member of the faculty of a U. S. medical school to undertake study in the Far East that will increase his effectiveness as a medical educator. The fellowship will provide for study and travel expenses and also a stipend as decided by the Award Committee. To be eligible, a candidate must (1) be a citizen of the U. S., at least 30 years of age and not more than 55 years of age when the proposed project is due to start; (2) hold a full-time position on the faculty of a medical school in the U. S. and be recommended by the dean of the institution; (3) in general, be willing to devote a minimum of 4 months full time to the study project (maximum period 12 months) and spend a significant amount of time in one place; (4) submit a written statement of what he proposes to do if awarded a fellowship (confirmation must be obtained from the foreign institution acting as host that the candidate is acceptable and that suitable facilities are available for his use); and (5) a personal interview will be required. Projects must be concerned with the areas of the board's interest in the Far East, i. e., South Korea, Japan, Taiwan, Hong Kong, Philippines, South Vietnam, Thailand, Malaya, Indonesia, Burma. In general, awards will include funds for travel for the fellow and his wife, study expenses, and a stipend commensurate with the individual's salary, if this is not continued by the institution where he is connected. For trips of nine months or longer, travel funds also will be provided for the fellow's children under 21. Applications for 1960 fellowships should be submitted before April 15, with the Director, China Medical Board of New York, Inc., 30 E. 60th St., New York 22. Applications for the fellowship to begin during 1961 must be submitted prior to Dec. 31, 1960.

LATIN AMERICA

Congress of Gastroenterology in Santiago.—The Seventh Panamerican Congress of Gastroenterology, under the sponsorship of the Interamerican Association of Gastroenterology and the Chilean Society of Gastroenterology, will be held in Santiago (Chile) Oct. 23-29. The main themes of the congress will be (1) diagnosis of hepatic cirrhosis, (2) treatment of hepatic cirrhosis, (3) physiology and pathology of the small bowel, and (4) cancer of the colon, rectum, and anus. Panel discussions and lectures will be arranged in connection with these themes. Scientific and technical-commercial exhibits will be organized. Other gastroenterological subjects, either clinical or in the basic sciences, are invited for submission and will be accepted for presentation if approved by the Scientific Program Committee. Simultaneous translations will be provided for Spanish and English. Registration fees are $25 for full members and $10, social registration. Information may be obtained from the Congress Office: Dr. Ricardo Katz, Hospital del Salvador, Casillar 70-D, Santiago, Chile.

FOREIGN

South African Pediatricians Change Address.—The South African Paediatric Association announced that its new address is: % Dept. of Child Health, University of Cape Town, Medical School, Mowbray, Cape Town, South Africa.

CORRECTION

Hospital Has 119 Ward Beds.—Dr. Harry H. Gordon, pediatrician-in-chief, Sinai Hospital, Baltimore, has written that an error appeared in the Medical News item headed "Hospital Plans to Move," J. A. M. A. 171:2106 (Dec. 12) 1959. The statement "There are 19 ward beds" should read "There are 119 ward beds."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for filing application was January 10. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Internal Medicine: *Oral.* San Francisco, March 30-April 1; New York City, Nov. 14-17. Closing date for filing application is Jan. 2 and July 1. *Written.* Oct. 17. Closing date for filing application is May 1. *Oral. Gastroenterology.* Philadelphia, March 11-12. Final date for filing application was January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* January 1960 in various cities. Applications for the 1960 written *examination must be filed before July 1. Oral.* San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral,* Chicago, Oct. 3-7. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. *Final date for filing application* is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Cincinnati, Spring 1960. Deadline for filing applications was Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Oral Examinations (Part II):* New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Feb. 12. Final date for filing application was Dec. 1. *Oral.* May 1960. Final date for filing application was *Dec. 1. Sec., Dr. Wm. M. Tuttle, 1151* Taylor Ave., Detroit 2.

American Board of Urology: *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

ARMY

New Vaccine Against Respiratory Diseases.—In the near future adenovirus vaccine will be given to all recruits. Although this is not the long-sought cold prevention vaccine, tests have shown that it protects these men against adenovirus-caused respiratory infections, which account for 50% of time lost from duty due to disease in recruits. Although the disease is not fatal, 5 to 10% of adenovirus infections among recruits develop into mild pneumonia. Since 1954 over 16 different adenovirus strains have been isolated. Only two of these, types 4 and 7, are of major importance among recruits. These types do not cause epidemics among either seasoned troops or civilians.

NAVY

Change of Duties.—Capt. Malcolm W. Arnold has been reassigned in the bureau of medicine and surgery as director, professional division, succeeding Capt. Eugene V. Jobe, who retired from active service in November after more than 29 years of service. Captain Arnold moves to his new assignment from duty as head of the bureau's training branch, where he was replaced by Capt. John W. Albrittain.

PUBLIC HEALTH SERVICE

Danger in Trailer Heaters.—State health officers have been urged to warn owners of travel trailers equipped with a small bottled gas heater that such heaters apparently caused eight deaths within the last few weeks. The heater is the "Thurm Heater" manufactured by the Thurm Engineering Company of Elkhart, Ind. It is a wall panel unit which burns bottled gas and which, because of its faulty design, is capable of building up a lethal concentration of carbon monoxide gas within a trailer in a short time, under normal operating conditions. Some 2,000 of the heaters have been installed in trailers in the last 18 months. The heaters were sold to trailer manufacturers and dealers but the large number of these firms makes difficult the problem of tracking down each trailer now equipped with the model in question. Local radio broadcasts and the use of State highway police patrols and game wardens may be the only way to reach many hunters and campers. The same company also manufactures a larger heater of the same general design, but this heater has not been implicated in any of the incidents thus far reported.

Training in Epidemiology.—A course in applied epidemiology will be offered at the Communicable Disease Center, Atlanta, Ga., May 9-13, 1960. This course is designed primarily for physicians who serve as investigators of disease outbreaks or have administrative responsibility for such investigations. It serves both as a refresher course for experienced health administrators and as an introductory course for physicians new to public health. Emphasis is placed on developing an understanding of how epidemiologic techniques can be used in the approach to the solution of problems in the preventable disease field. Group participation is obtained through use of the group solution of epidemiologic problems, seminar-type presentations and panel discussions. Registrants will be expected to attend all sessions of the course. Further information and application forms may be obtained from the chief of the Communicable Disease Center Public Health Service, 50 Seventh St., N. E., Atlanta 23, Ga., to the attention of the chief of the training branch.

Personal.—Dr. Frederick J. Brady was appointed assistant director, office of public health, of th International Cooperation Administration in Washington, effective Nov. 1, succeeding Dr. Charle L. Williams Jr., who assumed the duties of chie of the health division, Lima, Peru.

FEDERAL AVIATION AGENCY

Civil Aeromedical Research Center.—The Federa Aviation Agency plans to build a Civil Aeromedica Research Center in Oklahoma City, at their aeronautical center at Will Rogers Field. The basi objective of the new center will be to develop th significant scientific data necessary to further promote air safety for pilots, air crews, and passengers The research will stress the development of th medical data necessary to meet anticipated operational problems as civil air operations move into higher altitudes and greater speeds. Included in this research would be studies of oxygen system for high-altitude aircraft, escape and survival procedures, effects of aging on the proficiency of airmen, prevention of injuries by improved design of aircraft interiors, and development of psychological tests to aid in selection of air traffic controllers. Plans call for completion of the new facilities by June 30, 1961. In the interim, personnel will be housed in the FAA Aeronautica Center facilities in Oklahoma City.

Personal.—Dr. Bennie A. Moxness was appointed chief of the examiner training and control branch in the office of the civil air surgeon.

DEATHS

Bayer, Bernard Hyman Ⓜ Houston, Texas; Tulane University School of Medicine, New Orleans, 1935; interned at the Houston Tuberculosis Hospital and the Jefferson Davis Hospital, Houston, where he also served a residency; past-president of Phi Lambda Kappa; past-president, vice-president, and chairman of the board of the Harris County Academy of General Practice; former secretary-treasurer of the Texas Academy of General Practice; member of the Southern Medical Association, Post-Graduate Medical Assembly of South Texas, Association of American Physicians and Surgeons, and American Academy of General Practice; president and general manager of Heights Medical Building; formerly instructor in urology at Baylor University College of Medicine; surgeon for the Southern Pacific, Missouri Pacific, and Chicago and Eastern railroads; veteran of World War II; affiliated with Heights Hospital and Houston Negro Hospital; died Oct. 9, aged 48.

Beal, B. Clyde Ⓜ Clearwater, Kan.; born in Tama, Iowa, June 24, 1876; University Medical College of Kansas City, Mo., 1902; also a registered pharmacist; honored for fifty years of medical practice at the first Clearwater Community Homecoming in October, 1952; on the staff of the Wichita–St. Joseph Hospital, Wichita, where he died Oct. 14, aged 83.

Blakeney, A. Lanthus, Newtonville, Ala.; Chattanooga (Tenn.) Medical College, 1907; member of the Fayette County Hospital Board; died Oct. 6, aged 76.

Breck, Charles Arthur Ⓜ Wallingford, Conn.; Yale University School of Medicine, New Haven, 1930; interned at New Haven (Conn.) Hospital; during World War II served as a colonel with the Yale Medical Unit; at one time director of the alumni fund; formerly on the staff at his alma mater; died at Grace–New Haven Hospital Oct. 2, aged 54.

Bristow, Arthur Shaw Ⓜ Princeton, Mo.; Rush Medical College, Chicago, 1917; interned at Presbyterian Hospital, Chicago; member of the A. M. A. House of Delegates 1953-1956; president of the Missouri State Medical Association in 1945 and the Mississippi Valley Medical Society 1955-1956; on the staff of Wright Memorial Hospital, Trenton, Mo.; died in Kansas City, Mo., Oct. 15, aged 67.

Bruton, Leander Dresden, Muskogee, Okla.; born in Seymour, Mo., June 19, 1870; Barnes Medical College, St. Louis, 1897; for a time practiced in Hartville, Mo., and Tampico and Clovis, N.M.; on the staffs of the Oklahoma Baptist Hospital and the Muskogee General Hospital, where he died Oct. 13, aged 89.

Burnett, Ezra Ⓜ Delphos, Ohio; born in Jennings Township, Jan. 29, 1868; Ohio Medical University, Columbus, 1893; at one time practiced in Wetzel; past-president of the Allen County Medical Association; charter member and past-president of the Endocrine Study Club of Lima; former president of the Delphos Board of Education; surgeon for the Nickel Plate and Akron, Canton and Youngstown railroads; city health officer for many years; president and board member of the Delphos Citizens Federal Savings & Loan Company; affiliated with St. Rita's Hospital and Memorial Hospital, Lima, where he died Oct. 9, aged 91.

Cadbury, William Warder, Moorestown, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1902; former medical missionary in China, where he helped establish the Medical School at Lingnan University, served as professor of medicine, and was superintendent of Canton Hospital; former chairman of the International Red Cross Committee in Canton; at one time instructor of pathology at his alma mater and pathologist at St. Mary's Hospital, Philadelphia; member of the American College of Physicians; a minister in the Society of Friends and a director of the Chinese Christian Church and Center, Philadelphia; curator of ferns at the Academy of Natural Sciences and affiliated with the University of Pennsylvania Museum, Philadelphia; died in Friends Hospital, Philadelphia, Oct. 15, aged 83.

Chambers, Harry Leslie Ⓜ Lawrence, Kan.; born in Lacygne, Kan., June 12, 1869; Kansas City (Mo.) Medical College, 1895; in 1922 a member of the A. M. A. House of Delegates; former secretary of the Kansas Medical Society; died Oct. 9 in Little Rock, Ark., aged 90.

Chandler, Isaac Wayne Ⓜ Decatur, Ga.; Atlanta (Ga.) College of Physicians and Surgeons, 1909; formerly practiced in Avon Park, Fla.; past-president of the Florida State Board of Medical Examiners and the Tri-County (Highlands–Hardee–Desoto, Fla.) Medical Association; died Oct. 5, aged 79.

Congdon, Russell Thompson Ⓜ Wenatchee, Wash.; Harvard Medical School, Boston, 1907; member of the American College of Surgeons; in 1952 named Pioneer Honor Citizen of Wenatchee in recognition

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Ⓜ Indicates Member of the American Medical Association.

of his being an outstanding physician and surgeon and as an ornithologist of international fame; past-president of the North Central Washington Museum; author of "Our Beautiful Western Birds"; died Oct. 5, aged 79.

Cotham, Christian M. Ⓜ San Antonio, Texas; University of Texas Medical Branch, Galveston, 1909; member of the International College of Surgeons, the Southern Medical Association, and the American Academy of General Practice; on the staffs of Baptist Memorial, Nix, and Medical Arts hospitals, and Santa Rosa Hospital, where he died Oct. 3, aged 72.

Cummins, Joseph Layton Ⓜ College Place, Wash.; College of Medical Evangelists, Loma Linda–Los Angeles, 1941; interned at the Seattle General Hospital; served a residency at the Kern General Hospital, Bakersfield, Calif.; died in Long Beach, Wash., Sept. 18, aged 56.

Hahn, E. Vernon Ⓜ Indianapolis; Indiana University School of Medicine, Bloomington–Indianapolis, 1920; served a residency at the Robert W. Long Hospital, Indianapolis; president of the Indianapolis Medical Society in 1946-1947; on the boards of examiners of the American Psychiatric Association and the American College of Surgeons; member of Phi Beta Kappa, the Congress of Neurological Surgeons, the American Academy of Neurology, and the Central Neuropsychiatric Association; awarded the Ravdin Medal for scholarship; former member of the advisory committee of the State Health Department; clinical professor of psychiatry at his alma mater; president of the staff of Methodist Hospital; died Oct. 16, aged 68.

Heinold, Fred William Ⓜ Cincinnati; University of Cincinnati College of Medicine, 1924; interned at Cincinnati General Hospital; for many years president of the Cincinnati Board of Education; in 1957 president of the Ohio State School Board Association; past-president of the Southwestern Ohio District Board of Education; during World War II served as chairman of Red Cross safety services; past-president of the University of Cincinnati College of Medicine Alumni Association; on the staffs of the Deaconess, Bethesda, and Maple Knoll hospitals; died Oct. 20, aged 62.

Heller, James Daniel Ⓜ Coplay, Pa.; University of Louisville (Ky.) School of Medicine, 1936; interned at Sacred Heart Hospital, Allentown, Pa.; served during World War II as a flight surgeon; member of Phi Chi; on the staff of Sacred Heart Hospital, where he died Oct. 21, aged 48.

Hughes, Albert R., Miami, Okla.; born in Mt. Grove, Mo., Aug. 24, 1869; licensed by years of practice; for a time practiced in Wyandotte; served as Ottawa County health physician; died Oct. 11, aged 90.

Jones, Augustus Benjamin, Jr. Ⓜ Bakersfield, Calif.; Georgetown University School of Medicine, Washington, D. C., 1946; interned at the Youngstown (Ohio) Hospital; served a residency at Letterman General Hospital, San Francisco; certified by the National Board of Medical Examiners in 1947; specialist certified by the American Board of Pathology; member of the College of American Pathologists; associated with Mercy Hospital; died Sept. 10, aged 39.

Keeney, Palmer Gunkel, Fort Thomas, Ky.; Medical College of Ohio, Cincinnati, 1899; for many years practiced in Newport and Bellevue, where he served as city physician; captain in the U. S. Army in World War I; died at the Veterans Administration Hospital, Cincinnati, Oct. 14, aged 82.

Lo Porto, Dominic Leo Ⓜ Albuquerque, N. M.; St. Louis University School of Medicine, 1930; interned at St. Thomas Hospital of Akron, Ohio; died Sept. 30, aged 54.

Melby, Benedik Ⓜ Bloomington Prairie, Minn.; University of Minnesota Medical School, Minneapolis, 1903; member of the American Academy of General Practice; on the board of education, 1916-1955; honored by his community for fifty years of practice in 1953; in February, 1951, awarded a scroll by the Minnesota Educational Association; died Oct. 11 at the St. Olaf Hospital, Austin, aged 82.

O'Brien, Edward James Ⓜ Detroit; born in Hatley, Wis., April 28, 1887; Wayne State University College of Medicine, Detroit, 1909; specialist certified by the American Board of Thoracic Surgery; clinical professor of surgery at his alma mater; past-president of the American Association for Thoracic Surgery and the American Academy of Tuberculosis Physicians; member of the American College of Surgeons, American Trudeau Society, and Central Surgical Society of Michigan; for many years chairman of the Michigan State Tuberculosis Sanatorium Commission; in 1952 given the Dr. Bruce H. Douglas Award, Michigan's highest honor, for his work against tuberculosis; in 1956 his portrait was hung in Herman Keifer Hospital, where he served as chief thoracic surgeon and later consultant; during World War I was a member of Base Hospital 17; originator of the collapsed lung operation for use in tuberculosis treatment; contributor to many medical journals; died Oct. 19 in Harper Hospital, where he had served a residency, aged 72.

Parker, Valeria Hopkins Ⓜ Greenwich, Conn.; born in Chicago in 1879; Hering Medical College, Chicago, 1902; past-president of the National Council of Women; in 1910-1911 served as chairman of the Connecticut Woman Suffrage Association; in June, 1921, was appointed executive secretary of the

United States Interdepartmental Social Hygiene Board, and for her work she received a letter of commendation from General of the Armies John J. Pershing; chairman of the Social Hygiene Committee of the League of Women Voters; director of the department of social morality of the Women's Christian Temperance Union; on the staff of the American Social Hygiene Association; first state policewoman in the U. S. and supervisor of state policewomen during World War I; past-chairman of the National Committee of Parent-Teachers Associations; at one time Greenwich probation officer; founder of the Institute of Marriage and the Home, East Orange, N. J.; author of "For Mothers and Daughters"; honorary member of the Greenwich Medical Society; died in Greenwich Hospital Oct. 25, aged 80.

Porter, Joel Lee Ⓜ Rutledge, Ga.; born in Jasper County, Ga., Jan. 8, 1882; Medical College of Georgia, Augusta, 1905; died in Newton County Hospital, Covington, Ga., Sept. 18, aged 77.

Tenaglia, Eutimio Domenico Ⓜ St. Louis; St. Louis University School of Medicine, 1928; interned at St. Mary's Hospital, Kansas City, Mo.; served a residency at Westmoreland Hospital, Greensburg, Pa.; at one time practiced in Providence, R. I.; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Oto-Laryngology and the American College of Surgeons; served with the Army Medical Corps in World War II; associate professor of clinical ophthalmology at his alma mater; on the staffs of Missouri Baptist Hospital, DePaul Hospital, and St. Mary's Group of Hospitals of St. Louis University; died in Moberly, Mo., Oct. 12, aged 58.

Townsend, Howard, Poughkeepsie, N. Y.; Cornell University Medical College, New York City, 1935; interned at Roosevelt Hospital, New York City; a founder of the visiting Nurse Service of Poughkeepsie; former senior attending physician at Vassar Brothers Hospital, where he died Oct. 23, aged 59.

Tupper, George Benjamin Ⓜ Cleveland; born near Genoa, N. Y., in 1881; New York University College of Medicine, New York City, 1910; interned at St. Luke's Hospital, Cleveland; at one time a high school principal in Bay Shore, N. Y.; chief district surgeon for the Pennsylvania Railroad from 1944 to 1954; member of the Cleveland Academy of Medicine; on the staffs of Woman's Hospital and St. Luke's Hospital, where he died Oct. 13, aged 78.

Vaccaro, Sebastian Pasquale, Interlaken, N. J.; Georgetown University School of Medicine, Washington, D. C., 1932; interned at Monmouth Memorial Hospital, Long Branch, N. J., and St. Mary Hospital, Hoboken, N. J.; recently was made a Knight of St. George by Pope John XXIII for his humanitarian services; died Oct. 21, aged 51.

Van Wagenen, Harry Parker Ⓜ Kingston, N. Y.; born in Creek Locks, N. Y., Feb. 15, 1874; State University of New York College of Medicine at New York City, Brooklyn, 1896; ward superviser for the city of Kingston; on the courtesy staff of Benedictine Hospital, where he died Oct. 22, aged 85.

Walsh, Thomas Nelson, Hawkeye, Iowa; born in Ormstown, Quebec, Canada, in 1864; McGill University Faculty of Medicine, Montreal, 1892; in 1943 was honored by the Fayette County Medical Society for fifty years of service and in 1952 was honored by the residents of Hawkeye; served during World War I; member of the school board; *died Oct. 15, aged 94.*

Ward, Edward Silvanus, North Attleboro, Mass.; born in Brookfield, Mass., Dec. 25, 1875; Harvard Medical School, Boston, 1903; during World War I was in charge of an Army base hospital in Bordeaux, France; for many years a welfare physician and a member of the board of health; on the staff of the Sturdy Memorial Hospital, Attleboro; died Sept. 30 in Bristol County Hospital, Attleboro, aged 83.

Wilhelm, George Thomas Ⓜ Knoxville, Tenn.; University of Tennessee College of Medicine, Memphis, 1917; served with the Army Medical Corps during World War I; in 1950 retired as health director at the University of Tennessee Infirmary and as professor of preventive medicine; former coordinator of the University of Tennessee Memorial Research Center and Hospital; at one time on the staff of the Campbell Clinic in Memphis; died in Presbyterian Hospital Oct. 16, aged 70.

Willis, Byrd Charles, Orange, Va.; Medical College of Virginia, Richmond, 1909; specialist certified by the American Board of Surgery; during World War I served at the Naval Hospital, Newport, R. I.; member of the Southern Surgical Association, the American Association for the Surgery of Trauma, and the American College of Surgeons; one of the principals of the Boice-Willis Clinic at Park View Hospital, where he was a consultant; a director of the Peoples Bank and Trust Company; died at the Medical College of Virginia Hospital, Richmond, Oct. 18, aged 79.

Wood, Charles, Westport, Ind.; University of Louisville (Ky.) School of Medicine, 1907; died Oct. 5, aged 79.

Young, Walter Henry Ⓜ Maywood, Ill.; Chicago Medical School, 1936; for four years central area physician for the American Can Company; died in Westlake Hospital, Melrose Park, Ill., Oct. 14, aged 52.

FOREIGN LETTERS

AUSTRALIA

Tremor Syndromes.—A new disease which is decimating the Fore people in the eastern highlands of Australian New Guinea was described last year (*J. A. M. A.* 166:1078). Several reports on this disease, known as kuru (meaning "the shakes"), have since appeared. It manifested itself in the form of severe tremors, which increased in severity, prevented walking or standing, and made speech unintelligible. Dysphagia and urinary and fecal incontinence ultimately resulted in death. The patients remained remarkably euphoric throughout the illness. The disease affected only the Fore people and those who intermarried with them.

Another tremor syndrome affecting the Wabag-Lacagam-Kundep region of the eastern highlands of Australian New Guinea has now been described by Wilson and co-workers (*Lancet* 2:699, 1959). This disease, known by the people as puriripiram or sometimes as waruwaru (the shivers), showed a marked similarity to kuru in some patients. In others it resembled paralysis agitans. No neuropathological examinations have been possible because no fatal cases have yet been seen. So far Wilson and co-workers have seen 24 patients with the new tremor syndrome. Males were predominantly affected (there were only two females). The youngest patient was aged 16 and the oldest 70 years. In a typical case the patient suffered from a generalized coarse tremor which became progressively more severe. Walking, with a swaying ataxic gait and extreme tremor, was possible only with the feet wide apart. The patient reeled, swayed, and staggered as if inebriated, and many of his movements were choreiform. The Romberg test result was positive when the patient's eyes were open, the finger-to-finger and finger-to-nose test results were poor, and the deep tendon reflexes were hyperreactive. Cranial and sensory nerves were intact and nystagmus was absent. The spinal fluid was normal. Unlike kuru this form of the disease might last for many years. Some forms, however, closely resembled kuru and were rapidly progressive.

BRAZIL

Visceral Leishmaniasis.—The epidemiologic data on visceral leishmaniasis in the state of Minas Gerais were analyzed by Dr. Celso Oliveira and co-workers (*Hospital,* vol. 56, October, 1959) who found that dogs were an important reservoir of Leishmania donovani. In man leishmaniasis is more common in children than in adults and more common in boys than in girls. Control measures included the early diagnosis and treatment of human cases, elimination of infected dogs, and suppression of the insect vector. The diagnosis in dogs was made by use of a complement-fixation test and the examination of Giemsa-stained smears of the skin of the ear. The complement-fixation test, however, was the method of choice, because it revealed recent infections or infections with little skin parasitism. The insect vector was the Phlebotomus longipalpis.

INDIA

Nutritional Edema.—Goswami and Barua (*Indian J. Pediat.,* vol. 26, July, 1959) stated that the role of serum protein in the production of edema has been questioned, as some patients have had massive edema although the serum protein concentration was above the critical level, while others with low protein concentrations had no edema. The authors carried out paper electrophoretic analysis of the serum proteins of 32 patients with nutritional edema. No patient with malignant edema or kwashiorkor was included in this study. The age of these patients varied between 10 and 29 years. The authors found a lowering of the total serum protein and the serum albumin levels while the rest of the components were within the normal range. The alpha-1, alpha-2, and beta globulin levels were either normal or slightly above normal. The gamma globulin level, however, showed a constant increase whenever there was a lowering of the serum albumin level. The gamma globulin level was independent of the level of total serum proteins. No definite correlation was seen between the production of edema and the level of total serum proteins or its components.

Obstacles to Health Plan.—The World Health Organization for Southeast Asia reported that the public health program in the region suffered from several deficiencies which could be removed only if the limited resources of the countries in the region are used judiciously and a strict order of priorities is laid down. Although so-called health centers have been built at great cost, little has been done at these centers to improve sanitation or give proper health education, especially in nutrition. There is little enthusiasm about improving sanita-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

tion, despite the fact that a large proportion of the children are afflicted with intestinal worms and gastrointestinal infections. The sad state of sanitation in this region is reflected in the epidemics of cholera in Nepal, Thailand, and Calcutta in 1958.

While deploring the acute shortage of doctors and nurses in these countries, the report said they commonly spend their time on tasks that could be done more efficiently and economically by clerks or domestic workers. The report deplored the tendency to build new medical schools and double admissions to existing schools without providing adequate teaching staffs at the same time. Costly medical equipment, especially x-ray units and other apparatus, is frequently out of service because of lack of proper maintenance. Public institutions possess millions of dollars worth of such costly equipment, and yet hardly any of them are operated by properly trained technicians. Despite this, southeast Asian countries are making heroic efforts against tremendous odds to improve the health of their people. These efforts have resulted in some expansion of public health programs in the face of economic difficulties.

Home Treatment for Tuberculosis.—The results of a study in tuberculosis control in Madras indicated the possibility of a successful mass treatment of the disease without sending the patients to hospital. A summary of the methods adopted were reported by the World Health Organization. The report concluded, "Provided it can be shown that relapse is infrequent and that there is no special risk if patients are treated at home, and provided that the results of this study will apply in other communities, there may be little to gain from admitting the general run of patients to a sanatorium."

Induction of Labor with Oxytocin Injection.—John and Pandey (*J. Obst. & Gynec., India,* vol. 10, September, 1959) induced labor in 115 women with the use of an intravenous drip containing oxytocin injection. The drip was started after preliminary sedation with chloral hydrate. Oxytocin injection was added to an infusion of dextrose in saline solution after it had run in for 15 minutes at a rate of 15 drops per minute. The rate was then gradually increased to a maximum of 60 drops per minute. The drip was continued until the placenta was expelled, except in two cases. The indications for induction of labor were premature rupture of membranes in 31 patients, preeclampsia and eclampsia in 7, placenta praevia in 4, abruptio placentae in 1, hydramnios in 2, and elective induction in 70. The women in the last group were near term and complained of abdominal pain due to some intestinal disorder. The cervix was soft with 1 to 2 cm. of dilatation, and the pelvis was such that normal delivery was probable. In 64 patients the membranes were ruptured artificially before the drip was started, in 33 there was spontaneous rupture, and in 18 the membranes were intact. The drip was successful in 95.7% of the patients. The average amount of oxytocin injection used for completion of labor was 3.5 units (range 1 to 9.1).

In the three patients with eclampsia in whom labor did not start after two or three days of convulsions, the drip was successful in inducing labor, while in only two of the four patients with preeclampsia was the drip successful. When the membranes were ruptured labor could be successfully induced in 98.4%, while it could be induced in only 83.3% when the membranes were intact. The duration of labor was definitely shortened by the use of the drip. Fetal death was not attributable to the use of the drip in any of the cases. When stillbirth occurred, the fetus had died in utero before the drip was started. The blood pressure was not raised by the drip even in the patients with toxemia. The postpartum blood loss showed an apparent increase in only two patients. Complications were few. In one patient with edema of the cervix and in one with nondilatation of the cervix cesarean section was necessary. There were no maternal deaths. Elective induction with oxytocin drip is thus a safe procedure if the patients are selected properly and are under constant observation.

Anemia in Children.—K. J. Vyas (*Indian Practitioner,* vol. 12, September, 1959) stated that iron deficiency anemia is common among children here. This is especially evident in the first few years of life, with the two most frequent causes being infection and dietary deficiency. Iron given orally is effective in such patients unless they have an intolerance for it or there is failure of utilization of ingested iron. In such patients iron should be given parenterally. The intravenous route gives a quicker response than the intramuscular route. The author gave iron combined with a wide-spectrum antibiotic intravenously to a series of 20 children with anemia of infectious origin. The iron was diluted with 10 cc. of a 5% dextrose solution and was given slowly. No other hematinics were used. Oxytetracycline was given simultaneously in suitable doses either as syrup or capsule, and the erythrocyte count and hemoglobin values were determined every fifth day.

The hemoglobin levels showed an increase in 19 patients. One patient with chronic upper respiratory infection and rheumatic carditis failed to respond. Of those responding, 13 had a rise of more than 4%. The erythrocyte count also showed an increase in all 19 patients. All of the children in this study also suffered from malnutrition, and the addition of a high protein diet with vitamin therapy would probably have produced better results. There was not a single instance of toxicity from the iron given in this way.

Malignant Synovioma.—Sayed and Sahgal (*Indian J. Surg.*, vol. 21, August, 1959) observed a series of six patients (one man and five women) with malignant synovioma, a relatively rare tumor. Of these, two tumors were in the leg, one was in the thigh, one was in the arm, one was in the index finger, and one was in the pubic ramus. The age of these patients varied from 25 to 52 years. The duration of symptoms was short, varying from 4 to 10 months, except in one in whom the tumor had been present for two years. Pain was a frequent complaint. The tumors were generally large. The cut surface was pale and homogeneous with hemorrhagic areas. Microscopically some resembled fibrosarcomas and some adenocarcinomas, and in some the stroma showed dense collagen with hyalinization resembling cartilaginous or osteoid tissue. The apparent rarity of these tumors might be due to difficulties in diagnosis, as they could easily be mistaken for fibrosarcoma, mesotheliomas, or metastatic carcinomas. Correct diagnosis is, however, essential for proper prognosis and treatment. These tumors are highly malignant.

Threatened Abortions.—M. K. K. Menon and co-workers (*J. Obst. & Gynec., India*, vol. 10, September, 1959) examined vaginal smears and cervical mucus in a series of 252 unselected consecutive patients with threatened abortion in whom no obvious etiological factor could be found. The cervical smears were graded according to the degree of arborization. A differential count was made in vaginal smears to determine the number of eosinophils or mature cells and basophils. Greater emphasis was placed on the morphologic characters of the cells than on the staining property alone. A smear with more than 30% eosinophils was taken as estrogenic and believed to indicate a deficiency of progesterone. Pregnanediol estimations in 24-hour collections of urine were also made in most cases. Twenty-four patients proved to be not pregnant but to have a secondary amenorrhea; 185 patients were studied in detail and, of these, 154 were random, 12 were primary, and 19 were secondary habitual aborters. Of the random aborters 54.5% were in the first trimester and the rest were in the 12th to 24th weeks of their pregnancy.

The presence of ferning in the cervical smear, whatever its grade, always indicated a poor prognosis, and more than 80% of the patients with whom it was associated had abortions. Of the 154 patients, 65 showed an estrogenic vaginal smear with different grades of ferning and 54 of these aborted. The pregnanediol concentration in urine was estimated in 29 random aborters. Of these, 22 had a low pregnanediol level for their period of pregnancy and 17 aborted. Thirteen of those with a low pregnanediol level had a positive fern pattern in the cervical mucus, and 18 had an estrogenic smear. Only five had a normal smear and one of these aborted. Of seven patients with a normal pregnanediol level three aborted. None of these showed ferning, but the three who aborted had an estrogenic smear. Thus, while a low pregnanediol level indicated a bad prognosis in threatened abortion, normal values did not guarantee a good prognosis. A definite correlation was, however, noted between the pregnanediol level, vaginal cytological findings, and cervical mucus ferning. In a significant number of patients a low pregnanediol level was associated with an estrogenic vaginal smear and cervical ferning.

The random aborters were divided into two groups for purposes of treatment—one group, who served as controls, received only rest in bed, sedatives, and orally given iron. The other group was given 5 mg. of diethylstilbestrol orally three times a day in addition, and in these patients changes in cervical mucus and vaginal smears progressed until the pregnancy either ended in abortion or went on to term. If the pregnancy continued, diethylstilbestrol treatment was stopped after 24 weeks of pregnancy. Fifty-seven patients were thus treated with diethylstilbestrol. Of these, 32 aborted, while 87 of the 97 patients who served as controls aborted. Forty-seven patients with normal smears and cervical mucus were not given hormone, and 29 of these aborted; of 45 similar patients treated with diethylstilbestrol 10 aborted. Thus, with a normal vaginal cytology and cervical mucus, administration of diethylstilbestrol helped to reduce the rate of abortion. It was of little use in patients with abnormal cytological findings, cervical mucus, or both.

Griseofulvin for Ringworm.—S. C. Desai (*Indian J. Dermat. & Venereol.*, vol. 25, July-Sept. 1959) treated 10 patients who had chronic cutaneous infections due to Trichophyton rubrum with griseofulvin. About 95% of adult ringworm is due to T. rubrum, which organism is highly resistant to local therapy. Results were assessed by noting the disappearance of erythema, itching, and infiltrative lesions. The duration of treatment was controlled by direct examination of scrapings from subsiding lesions on alternate days to follow the microscopic changes in the fungus due to treatment. The earliest period of cessation of treatment was 15 days, while some were treated for 22 days. All the patients showed a dramatic improvement within the first week, with reduction of intense itching within the first 24 hours in most of them. Mild itching persisted for varying periods up to 15 days. Mild erythema showed a reduction in 24 to 48 hours and subsided completely in five to eight days. Infiltrative nodules disappeared in 8 to 10 days in most and within 15 days in all patients. Two patients had a recurrence of itching after stopping the treatment for 20 days, and one had recurrence after 10 days.

Children, on the whole, required earlier cessation of treatment. Two patients with concomitant nail infection received treatment for 78 and 90 days, respectively, but the dose was reduced after the skin lesions had healed. No toxic side-effects were noted. Mycological examination showed breaking down to hyphae on the second to fourth day except in one patient in whom it occurred on the eighth day. The results were satisfactory clinically, although some recurrence was noted. The drug has pronounced activity against the mycelian phase of T. rubrum while the spores persist and may even increase, which may be one of the reasons for recurrence.

Surgical Treatment of Duodenal Ulcer.—D. M. Hancock and co-workers (*Indian J. Surg.*, vol. 21, August, 1959) stated that the advantages of segmental resection in the treatment of duodenal ulcer are that the nutritional results are better, sideropenic anemia does not occur, and the early and late postcibal syndromes are less marked. Weight loss, however, was a frequent complication. The procedure includes excision of a large part of the acid-secreting area of the stomach, with retention of the pyloric antrum, performance of an extra-wide Heineke-Mickulicz pyloroplasty, and restoration of gastroduodenal continuity. The authors found the results with this operation satisfactory for active indurated penetrating and obstructing duodenal ulcers, but in order to avoid weight loss some modifications were tried in a series of 42 patients.

In group 1 (4 patients) segmental resection was combined with vagotomy and the full width of the gastric fundus was anastomosed to the antrum. In group 2 (14 patients) the above procedure was performed without vagotomy. In experimental studies it was noticed that the addition of vagotomy to segmental resection predisposed to histamine-induced ulceration. In group 3 (five patients) tubular resection was performed, with transverse gastroplasty. In group 4 (six patients) the greater curvature was used for anastomosis after resection. In group 5 (13 patients) segmental resection was performed with use of the lesser curvature.

After resection, the fundic stump left behind was equivalent to 30% and the antral pouch was equivalent to 20% of the stomach. The stomach was thus reduced to about 50% of its preoperative size. There were no deaths. In a series of patients treated by older methods, who were studied for comparison, there was a high incidence of radiation of pain to the back and of obstructive vomiting. Food usually aggravated the pain, which was then relieved by vomiting. The modification of segmental resection with use of the lesser curvature (group 5) was found to be a definite improvement on other types of conservative segmental resection. Parietal cell counting and studies of vascular anatomy indicate that the lesser curvature and cardiac area of the fundus play only a minor role in acid production as compared to the greater curvature. Excision of the greater and retention of the lesser curvature is therefore a better method for formation of the fundic pouch.

Schistosomiasis.—Schistosomiasis has been prevalent in Egypt, Japan, and Brazil but unknown in India until recently, when it was found in an endemic form in some areas on the western coast. A snail known as Ferrissia tenius is the intermediate host. Until now only two types of snail, the Bullinus and Physopsis, were known to act as hosts of the parasite.

NORWAY

Addiction to Barbiturates.—Dr. E. Kåss and co-workers (*Nord. med.*, Oct. 8, 1959) reported a series of 207 consecutive cases of drug poisoning. Of these, 81 women and 56 men had taken barbiturates in toxic amounts and 37 were associated with alcohol poisoning. Seven patients died, and 17 probably owed their lives to the treatment they received. Among the 60 patients found to be addicts 43 were addicted to barbiturates alone and in 17 barbiturate addiction was combined with addiction to other drugs. In 15 the addiction followed the prescription of a barbiturate by a physician. The authors concluded that barbiturates are the most common source of drug addition in patients coming under medical treatment, that other drugs should replace them in the treatment of insomnia, and that special care should be taken not to prescribe barbiturates for alcoholics.

A Plea for Placebo Tablets.—While the pharmacists attached to hospitals can supply staff members with placebo tablets for controlled studies of new drugs and the study of psychotherapy, the general practitioner often lacks such tablets. For this reason Dr. A. Fugelli (*Tidsskr. norske laegefor.*, Oct. 1, 1959) urged manufacturing chemists to provide such tablets. He believed that five to eight different types of placebo tablets could be put on the market, each with its special name, packing, color, and shape. With their help the consumption of sedatives, hypnotics, and ataraxics could be reduced, a certain economy effected, and much learned about the power of suggestion.

Dr. Fugelli's advocacy of placebos drew an emphatic protest from Dr. Ramsfjell (*Tidsskr. norske laegefor.*, Nov. 1, 1959) who argued that an intolerable state of affairs would be created if the medical profession were to make extensive use of placebos, equipped with fancy names, in the practice of psychotherapy. Mistrust is one of the most important obstacles to cooperation between human beings. No one needs the confidence of his fellow beings more than the physician. The treatment suggested would bring a cheap and brief improvement to some patients but would constitute a smoke screen and blur the outline between truth and falsehood. What would we say about members of other professions who used deception to promote confidence? If this treatment became general, it would lead medicine in the direction of quackery.

Promotion of Infections by Tranquilizers.—Dr. E. Ose (*Tidsskr. norske laegefor.*, Oct. 1, 1959) stated that, although the contribution of chlorpromazine to the treatment of mental patients in the past seven years has been epoch-making, its use is not without dangers. Advertisements for this drug and for perphenazine may mention leukemia as a contraindication, but they are silent about infections in this respect. In addition to reporting two patients with pneumonia, the grave course of whose illness may have been due to one or other of these drugs, the author noted that the death rate from acute infections had risen of late in his mental hospital. He concluded with the advice that neither of these drugs should be given when patients are febrile. An increased sedimentation rate should inspire caution in prescribing them.

SWEDEN

Esophageal Cancer.—A histological study by Frank Bergman (*Acta chir. scandinav.* 117:356-365, 1959) reported 10 patients with cancer of the esophagus who were surgically treated. The tumors were of the squamous cell type with good evidence of primary esophageal origin. In all specimens microscopic tumor growth was seen beyond the macroscopic border of the primary tumor. None of the patients had had symptoms for more than six months before admission to hospital. The tumors were detected by means of roentgenograms and esophagoscopy after which the diagnosis was verified by histological examination of a biopsy specimen. All the patients underwent resection of the lower esophagus and cardia. Histological examination of specimens regularly revealed more extensive growth, especially proximally, than was apparent from gross inspection. This submucosal spread, which in half of the patients extended up into the margin of resection, might help to explain the poor results of operation. Nothing suggested the occurrence of a multicentric tumor in any of these patients.

Subphrenic Abscess.—Jarl Wetterfors (*Acta chir. scandinav.* 117:388-408, 1959) observed a series of 101 patients with subphrenic abscess. Only three of the patients were children. The age incidence was maximal in the sixth decade, which denoted a further shift toward higher ages in comparison with earlier observations. In 60 patients the abscesses occurred as a postoperative complication. Biliary tract diseases and peptic ulcers were responsible for most of them. Acute appendicitis accounted for only 10%. In six patients the cause was unknown. In the patients in whom the mode of spread of infection to the subphrenic region could be investigated, it was found that the infection from such neighboring foci as ulcers and infected gallbladders always spread by the intraperitoneal route. A purulent streak or remnants of one extended from the focus of origin, in most instances via a subhepatic abscess or accumulation of exudate, to the subdiaphragmatic space around either the anterior or the lateral margin of the liver. This way of spread could be demonstrated in some patients with bilateral abscesses. Lymphatic spread was not verified in any of the patients. Such distant foci of origin as appendicitis or pelvic inflammation were present in 14. In 13 the abscess was occasioned by direct intraperitoneal spread or followed a general peritonitis. The abscesses occurred postoperatively in 15 patients.

In contrast to the observations of other workers, the author did not find that the mortality was affected by the length of time between the onset of the abscess and its drainage. The clinical findings in most patients were those of continued intra-abdominal infection with either a sudden or an insidious onset. The diagnosis was based primarily on radiological evidence. Conservative treatment with antibiotics used in the proper way and under radiographic control was effective. The drugs used were penicillin, streptomycin, chloramphenicol, oxytetracycline, and chlortetracycline. Of 27 patients treated with sulfonamides, the mortality was 46% in those operated on and 35% in those treated conservatively. Of 58 patients treated with antibiotics, the mortality was 40% in those operated on and 27% in those treated conservatively. Mortality was thus lower in the conservatively treated patients. The author concluded that if regression with absorption of the abscess did not seem to occur with conservative treatment surgical drainage should be instituted. This can then be performed at the stage of lowest possible virulence. Drainage should be made by the extraserous approach because this method involves the least risk of fatal intrathoracic and intra-abdominal complications.

Adrenal Autotransplantation.—Free autotransplantation of adrenal tissue in human subjects showed that cortical tissue but not medullary tissue survived the transplantation and that transplantation resulted in a great reduction of the amount of functioning cortical substance. C. Franksson and co-workers (*Acta chir. scandinav.* 117:409-415, 1959) performed adrenal autotransplantation in five women who had pituitary basophilism with diffuse hyperplasia of the adrenal cortexes. One or both adrenals constituted the transplant. The postoperative observation period ranged from three months to two years and four months. No serious complications occurred in association with the operation. The pituitary basophilism disappeared in all. Postoperative urinalysis revealed steroid metabolites which normally are present in the urine. This indicated that the transplant, assessed qualitatively, had a fairly normal steroid secretion. Quantitatively the urinary steroid values were below normal. Injection of ACTH was not followed by any marked increase in steroid excretion.

These findings were interpreted as showing that the transplants were maximally utilized even without extra stimulation. The best clinical result in this series occurred in the youngest patient (aged 24 years). The aim of surgery in this disease is to diminish the adrenal steroid values and thus cause the pathological manifestations to disappear. This result was accomplished by total adrenalectomy, which also rendered the patients totally dependent on exogenous steroids. Adrenal autotransplantation gave the advantages of subtotal adrenalectomy (low requirements of exogenous steroids) without its main disadvantage (risk of another major operation). In the present cases the postoperative levels of steroid secretion tended to be too low. It was therefore conceivable that the steroid secretion of transplants might increase when more time had elapsed after the operation. Refinements in transplantation technique might also improve the results in future cases. Should the function of the transplant become excessive, only a relatively simple operation would be required to remove more adrenal tissue.

UNITED KINGDOM

Lung Cancer in South Africa.—Impressed with the fact that he rarely saw a patient with bronchial carcinoma in Port Elizabeth, South Africa, although other forms of cancer appeared to be as common as in Britain, Dean analyzed the deaths from cancer of the lung among South African men for the period 1947 to 1956 (*Brit. M. J.* 2:852, 1959). The patients were classified according to age, country of birth, and place of residence. The low incidence of carcinoma was surprising because cigarettes cost only about 85 cents per 100 and most men appeared to be heavy smokers. Indeed, caucasoid South Africans have long been the heaviest cigarette smokers in the world. Among those dying between the ages of 45 and 65 years, British immigrants had a higher death rate from cancer of the lung than men born in the Union of South Africa or than immigrants from other countries.

As most of the British immigrants came to South Africa before reaching middle age, British cigarettes are likely to have formed only a small fraction of the total number of cigarettes smoked by those dying of lung cancer. It is therefore unlikely that the high lung cancer rate in British immigrants was due to smoking British cigarettes. No significant difference existed in the lung cancer rate between the British immigrants and native born South Africans after the age of 65 years. This suggests that the greater liability of the more recent British immigrants to lung cancer is a relatively new occurrence and that the immigrants had been exposed to the etiological factor before they left Britain.

There was a higher incidence of lung cancer among the residents of South African towns, and in Durban particularly, compared with the incidence among residents in rural areas. This supports the view that urbanization and industrialization, with their atmospheric pollution, are factors in the etiology of cancer of the lung.

Antibiotics from Coal.—At a meeting of the Association of Clinical Pathologists in London, Prof. W. D. Evans, of Nottingham, reported that carboniferous coals contain antibiotics derived from the bacterial decay of plants. They are collectively known as vitricin and appear to have some control over miner's pneumoconiosis. Coal dust containing a high concentration of the antibiotic occurs in mines where there is a low incidence of pneumoconiosis, and conversely. Among the organisms whose growth is inhibited by vitricin are Mycobacterium phlei, Staphylococcus aureus, Pseudomonas aeruginosa, and Mycobacterium tuberculosis. Guinea pig tests show that it is of low toxicity and inhibits the growth of tubercle bacilli in vivo. Sixteen compounds have been isolated from crude vitricin. Serial dilution tests show that the antibiotic is active at a concentration of 1:19,000,000 against Myco. phlei, but this activity is largely suppressed in the presence of serum. The antibiotic is also fungistatic and is active against Aspergillus niger and a number of other fungi.

Ovariectomy and Coronary Artery Disease.—The greater frequency of coronary artery disease in men than women is related to age, the sex difference largely disappearing between the ages of 60 and 70 years. Oliver and Boyd related this levelling out with age to the rise in serum cholesterol level in women after the age of 50 years and to hormonal changes after the menopause (*Lancet* 2:690, 1959). They determined the mean serum cholesterol level of 213 healthy women and classified the results into quinquennial age groups. There was a slight progressive rise with age from 20 to 50 years and after that a sharp rise, with a peak between 55 and 60 years of age. This rise in the serum cholesterol level in women in the sixth decade is not seen in men of the same age.

Since the peak incidence of coronary disease in women occurs about 15 years after the menopause, a further study was made to see if a premature menopause was followed by a significant change in the incidence of coronary artery disease or a rise in the blood cholesterol level. Women who had had both ovaries removed 20 or more years before the start of the investigation when they were aged 35 or less were followed up. No woman was older than 59 years of age at the time of the study. A random group of women seen in general practice and in the same age group was selected to serve as controls. The mean serum cholesterol level and the cholesterol phospholipid ratio were higher in those women who had undergone bilateral ovariectomy. As a group they also showed premature development of coronary artery disease. This was present in 25% compared with an incidence of 3.5% in the women seen in general practice; it was present in 3.2% of women who had undergone unilateral ovariectomy only. It would thus seem that ovarian estrogen excretion is inversely related to the development of coronary artery disease and to elevated serum lipids. The authors believe that for this reason estrogen replacement therapy should be given to women under 50 years of age who, for gynecologic reasons, have had both ovaries removed or irradiated.

Dialytic Parabiosis.—The drawbacks of the artificial kidney in the treatment of acute renal failure are well known. Not only are harmful substances such as urea removed by dialysis, but such essential substances as vitamins, coenzymes, amino acids, and trace elements also diffuse out of the patient's blood and are lost. The ideal treatment is cross-circulation from a donor, but this is seldom practicable. Pavone-Macaluso and Anello described an alternative treatment that they have termed dialytic parabiosis (Lancet 2:704, 1959). This technique, which has been compared with an artificial placenta, allows transfer between the recipient and donor, without any mixing of blood, across a dialyzing membrane of cellulose. This is permeable to water, electrolytes, urea, and small molecules but not to colloids such as proteins and antigenic substances. The bath fluid is a small volume of diluted plasma, the composition of which is kept constant by the donor, which, as the two bloods do not mix, may be of different species from the recipient. Thus plasma from a living dog, sheep, or horse may be used in the bath for a human recipient. The advantage of dialytic parabiosis is that the healthy donor, whose renal and other functions are normal, is able to react against any artificial changes. The donor removes harmful substances, such as urea, from the bath and can contribute essential factors to the bath for use by the recipient. The process is therefore of therapeutic value not only in the treatment of uremia but also in liver diseases in which the artificial kidney is of little value.

The method was used to treat a woman with uremia due to mercury poisoning. She had been anuric for 10 days. The donor was a large ewe, from which blood was obtained by the carotid artery. After circulating through the exchange bath it was returned to the jugular vein. The patient, who was in another room, was cannulated via the radial artery and a forearm vein. Both donor and recipient were heparinized. Owing to repeated falls in blood pressure the dialysis was stopped on the fifth day, when there was a diuresis of 2,300 ml. and the nonprotein nitrogen level started to fall. The patient made a complete recovery. In this particular case heparinization, although essential for the procedure, caused internal bleeding because of the hemorrhagic enteritis due to the mercury.

Preserving the Unfit.—In a speech at Southampton University Lord Adrian said that as the medical profession is saving many of the unfit the world must be prepared to accept more and more of them and the inheritance of factors likely to produce the unfit. This is one of the risks of progress. By diminishing early mortality we are preserving many unfavorable genes, which would otherwise have died out. A slow but sure genetic deterioration is taking place, and this may eventually make man unable to live in the world. Progress, Lord Adrian continued, is making the world more dangerous to live in. For example certain diseases, notably lung cancer, leukemia, and coronary thrombosis, are on the increase in civilized countries, and seem to be related to man's changed environment. Medical radiology is exposing the human gonads to a level of radiation more than 20 times as great as that due to atom bomb tests. Even in the examination of the heart and lungs, the gonads are exposed, unless they are especially shielded, to more radiation than they normally receive from natural sources. This could lead to the birth of a child with congenital defects and an increased tendency to leukemia. A sense of balance must be preserved, and actual gain must be set against possible loss. Radiography detects nearly 18,000 cases of tuberculosis annually, nearly 12,000 cardiac abnormalities, and 9,400 cases of pneumoconiosis. Every possible step should be taken to reduce exposure to radiation to a minimum.

CORRESPONDENCE

MASTER TWO-STEP EXERCISE TEST

To the Editor:—We read with interest the excellent paper, "Master Two-Step Exercise Test in Clinically Unselected Patients," by Dr. A. J. Brody, in The Journal, Oct. 31, page 1195. Brody's major conclusions deserve comment and, perhaps, amplification. It is gratifying that the value of a negative double two-step test result has again been demonstrated. In our experience, and that of other investigators, notably Robb and others (*Tr. A. Life Insurance M. Dir. America* 40:52, 1956) and Mattingly and others (Research Report 75-57, Walter Reed Army Institute of Research [May] 1957), a negative Master test practically, although not infallibly, excludes a diagnosis of myocardial ischemia at the time of testing. Brody's finding, that only 4.2% of his negative reactors subsequently developed coronary disease, closely parallels our own reports (Master: Proceedings of the Third World Congress of Cardiology, Brussels, 1958, p. 138; Master and others: Advances in Cardiology, New York, 1959, vol. 2, p. 243; read before the Vermont Heart Association and the University of Vermont College of Medicine, Burlington, Sept. 20, 1959; Master: Arthur C. Schaeffer Memorial Lecture, Millard Fillmore Hospital, Buffalo, N. Y., Oct. 13, 1959; read before the 68th annual meeting of the Association of Life Insurance Medical Directors of America, New York, Oct. 22, 1959). Of equal interest are Brody's criteria for a positive test result. We had previously stated that depressions of more than 0.5 mm. were considered positive, but, for the past two years, we have accepted mounting evidence that our original criteria were too rigorous. This became especially apparent with the increasing use of precordial electrocardiographic leads. We, too, have been focusing our attention on the configuration of the RS-T segment after exercise rather than merely on the extent of its depression in millimeters below the base line.

Dr. Brody's analysis of the configuration of the RS-T segment in the interpretation of the post two-step tracing is not a new approach. As early as 1943, Ashman (*Am. Heart J.* 26:495 [Oct.] 1943) commented on the different shapes of this segment and their possible significance. Other important work in this area was done by several investigators, notably by Wood and co-workers (*Brit. Heart J.* 12:363 [Oct.] 1950) in England (they in fact coined the term "ischemic RS-T segment") and Myers and Talmers (*Ann. Int. Med.* 43:361 [Aug.] 1955) in the United States, but it remained for Mattingly and co-workers to convey statistical validity to the meanings of the differently shaped RS-T depressions after exercise. So impressive were their findings, and so akin to our own subsequent clinical impressions, that we have stated in the past two years that, although every depression of RS-T must be suspect, the "junctional" type is probably of much less, if any, significance as compared to the horizontal or sagging "ischemic" configuration of RS-T. We no longer consider every depression of more than 0.5 mm. as necessarily abnormal.

Despite our confirmation of the observation that there is usually a difference in significance between "ischemic" and "junctional" depression, we were not prepared to dismiss the latter as innocuous in every instance. We believe there are further principles that must now be considered. As Brody quite correctly points out, in the classic work of Mattingly and others and Robb and others patients with the junctional responses had an incidence of coronary occlusion of 35 per 1,000 patient-years of observation. This figure is much less than the 79 per 1,000 incidence in ischemic tests but significantly higher than the 9 per 1,000 among negative reactors. Both groups of investigators obtained the same comparisons with death rates as with first occlusion rates. The "junctionals" are clearly a heterogenous group, so that some reflect the presence of myocardial ischemia while others do not. Brody states that these types may be distinguished from each other merely by the extent of their depression below the base line, but this is not so. The literature abounds with individual reports, each claiming a particular amount of RS-T segment depression to be the most reliable index of abnormality. We have found that while most junctional RS-T depressions are benign, about 25% are not, being present in patients with ischemic heart disease. Among this 25% of false-negatives, many are depressed less than 1.5 mm. below the base line.

We have recently analyzed 234 cases in which there was RS-T segment depression after the two-step test. The results of our experience were reported at recent meetings and are now being prepared for publication. Briefly, our findings indicate that of greater importance than the mere extent of RS-T segment depression is the duration of such depression in a given ventricular complex. Lepeschkin and Surawicz (*New England J. Med.* 258:511 [March 13] 1958) suggested a convenient technique of measuring such duration of RS-T depression in a given cardiac cycle, which we have found practicable and reliable. The time is measured in seconds from the beginning of the QRS complex to the point at which the depressed RS-T segment returns to isoelectricity. This time is expressed as a percentile of the Q-T interval in the same ventricular complex. A ratio of 50% or higher was found to be abnormal. There was an extremely high degree of accuracy in our 234 patients (especially among the men) who have been followed up between three and eight years, with an average of four years. With this technique of determining how long during electrical systole the RS-T segment remains depressed, we believe we have clarified considerably problems posed by interpretation of RS-T segments on the basis of morphology alone. We believe that the meaning of various forms of junctional depressions can now be more precisely determined. Such analysis of the RS-T segment is valid on physiological principles, according to which subendocardial ischemia might be expected to produce an injury current of greater duration, i. e., a more prolonged RS-T depression, than one expects with simple tachycardia or benign changes in ventricular gradient.

In summary, Dr. Brody's work serves to reemphasize the importance and practicality of the two-step test in the investigation of coronary heart disease. A negative response to a double test is especially revealing and even prognostic. Analysis of the positive response in terms of the configuration of the RS-T segment represents a major advance in the interpretation of the two-step test. It is our impression that measuring the duration of RS-T depression in a given ventricular complex is more accurate than the criteria heretofore set down.

We would caution readers about using one aspect of the technique used at the Greenbrier Clinic. It is not enough to record only the tracing taken immediately after exercise; in fact, in our experience, the greatest change in our patients occurs in the two-minute tracing. The immediate tracing is also the one most likely to be influenced by the effect of tachycardia. Again, the patient, having just completed the test, is more apt to breathe rapidly, causing wandering of the base line and increased difficulty in interpretation. We suspect that had Dr. Brody performed the test in the conventional manner, his results might have been even more revealing than they already are.

This paper from Greenbrier Clinic points out an important value of the standardized two-step test. It permits different investigators to compare results obtained in large numbers of persons. The amount and type of exercise is not administered at the whim of the individual examiner. When Brody states that 756 business executives performed the Master double two-step test, we know exactly what he means. We look forward to further reports from Brody and from others, and we are particularly eager to see whether the new technique we recommend for the evaluation of RS-T depression after the two-step exercise is as accurate in their hands as in our own.

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RADIOTHERAPY OF MALIGNANT DISEASE

To the Editor:—The article in The Journal, Sept. 12, page 133, entitled "New Horizons in Radiotherapy," is in general a paean in praise of "super"-high-voltage radiotherapy. However, the author, Prof. H. S. Kaplan, makes some statements which are so much at variance with clinical and physical facts that comment seems mandatory. He states that some data which he credits to, among others, G. H. Fletcher, "convincingly establish that supervoltage beams can eradicate deep-seated cancers more often than [can] conventional x-ray therapy." He seems to have forgotten the report of the conference on supervoltage techniques held at Highland Park, Ill., in May, 1957, published under his editorship as "Research in Radiology" by the National Academy of Sciences in 1958. Leading radiotherapists took part in this conference, and it was the consensus that there was no valid proof of improved cure rates with supervoltage, at least to that date. Indeed, Dr. Robert S. Stone observed that after almost 30 years of experience with supervoltage sources he believed "that these machines haven't accomplished very much except to make us pay more attention to our business" (page 141).

If short-term results of cancer therapy are to be published at all, they should be published from institutions in which both orthovoltage and megavoltage therapy are used for comparable groups and by the same team of therapists, who should approach as nearly as possible an attitude of objectivity. The first four of the following examples are results obtained under such circumstances: (1) carcinoma of the tonsil: five-year survival rates were 20% by orthovoltage, 20% by supervoltage (Sheline and others: *Am. J. Roentgenol.* 80:775 [Nov.] 1958); (2) carcinoma of the larynx: five-year survival rates with orthovoltage were 55%, with megavoltage 41% (Cantril: *Am. J. Roentgenol.* 81:456 [March] 1959); (3) carcinoma of the esophagus: many careful radiotherapists, notably Phillips at Memorial Hospital, Fletcher (*Am. J. Roentgenol.* 81:375 [March] 1959), and Friedman reported no difference in five-year survival rates for the two modalities; (4) carcinoma of bronchus: Fletcher and Phillips reported no difference in survival rates at the five-year level; (5) carcinoma of uterine cervix: in a noteworthy paper published in the *Nebraska State Medical Journal* (44:53 [Feb.] 1959), Hunt reported 60% five-year survivals in patients with stage-2 lesions treated with orthovoltage. Murphy, in his new textbook on radiation therapy (W. B. Saunders Company, 1959) reported 55% survival rate for five years when he relied on megavoltage (both authors used radium as well); (6) carcinoma of the bladder: Friedman, in *Radiology* (73:191 [Aug.] 1959), reported 13% five-year control with megavoltage sources and almost 56% when intracavitary sources were employed. These data fail conspicuously to support the notion that there is any superiority inherent in megavoltage sources.

Dr. Kaplan makes the plea for centralization of tumor therapy in cancer centers, since results will then be better than they are when patients are treated by "general" radiologists. This has a familiar ring. I think that it would be the opinion of your readers that well-trained general surgeons are competent to care for many cancer patients in the many widely separated cities and towns of this large country. The same is true for the increasing number of well-trained clinical radiologists, and while we must perforce operate under this system it is to be hoped that Dr. Kaplan is making some contribution to their education.

Of less importance, but indicative of something less than a passion for accuracy in Dr. Kaplan's paper, is the legend for figure 1, referring to "6 mev linear accelerator," and the curves in figure 2 comparing 6 mev depth doses with those from a conventional 200 kv. unit. Weissbluth, the distinguished physicist associated with Dr. Kaplan, published in the *Stanford Medical Bulletin* (15:210 [Aug.] 1957), that the unit operates at 4 mvp. The roentgen radiation from a 4 mvp outfit is further compared by Weissbluth with the radiation from a radiocobalt (Co^{60}) source, in a paper published in *Radiology* (72:242 [Feb.] 1959). The output from each has similar characteristics—and an approximate mev of 1.6.

The author fails to stress the great disadvantage of megavoltage irradiation in its early (apparent) skin-sparing effect, which leads to overdosage and a new spectrum of side-show sequelae such as fibrosis of panniculus and severe changes at the exit port. The devotee of the therapeutic high-energy band seems to lose sight of the one buttress of inexorable fact by which success or failure is determined with irradiation, i. e., the differential in effect on the neoplastic and the normal cell, otherwise known as radiosensitivity.

Everyone who essays to do radiotherapeutic work in cancer patients will periodically suffer from ego inflation, when confronted with an unexpected triumph in regression. Such miracles in defiance of usual natural history occur with treatment from a lowly 200 kv. unit just as often as with high-energy production of 20 mev or more. In each instance the flush of great achievement should be tempered by remembrance of the sage remark of a brilliant contemporary: "About 60% of the chance of controlling a cancer depends on the type and extent of the tumor (or biologic predeterminism), about 30% on the skill and experience of the radiotherapist, and only about 10% on the modality employed." It would be a disservice to your readers if the clinical and biological facts of radiotherapy were ignored.

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To the Editor:—The article on supervoltage radiotherapy in THE JOURNAL, Sept. 12, page 133, deserves some comment. The unit mentioned by the author is described in the radiologic literature as a 4-mvp unit and not, as published, a 6-mev unit. Any radiation physicist know the marked difference between the two terms. The effective voltage is reportedly 1.6 mev. The isodose curves are somewhat misleading, since lack of adequate depth dose is not the limiting factor in radiotherapeutic cure of deep-seated lesions; the limiting factors are lack of radiosensitivity, undue size of the tumor, and others. The data quoted from Fletcher and co-workers omit the important fact that they are not five-year survival rates. They are merely preliminary one-year, two-year, and three-year "controls" (*Am. J. Roentgenol.* 81:375 [March] 1959). As long as Fletcher was being quoted the author might have added these figures from the same article (table 3): Three-year survivals of patients with palatine arch cancers—52% with orthovoltage and 54% with supervoltage; not significantly different.

Comparative five-year survival rates with orthovoltage and megavoltage confirm the fact that, in practice, megavoltage does not offer any increase in rate of cure for most patients with neoplasms. It does offer increased hazard to the normal subcutaneous and deeper tissues, because the valuable warning of skin erythema is often absent. Cantril reported a higher five-year clinical cure rate of laryngeal cancer (55% with orthovoltage and 41% with supervoltage). Sheline reported no difference in cure rates of tonsillar cancer. Fletcher, Friedman, Phillips, and other radiotherapists reported no difference between orthovoltage and megavoltage treatment in control of esophageal or bronchial cancer. Hunt, with orthovoltage, secured better results in a series of patients with cervical cancer than any reported with megavoltage treatment. (References will be furnished on request.)

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These comments were referred to the author of the original article, whose reply follows.

To the Editor:—I will take the liberty of commenting on both letters together. They are similar in so many respects that they almost seem to have been written by the same person. Many of the points raised are matters of opinion, and I fear it will not be possible to provide evidence which would satisfy persons with the strong antisupervoltage bias reflected in these letters. The fact that neither of these physicians confines his practice to radiotherapy may have had an effect on their opinions on this subject.

Dr. Macdonald refers to the lack of statistical proof that supervoltage is more effective than conventional voltage in the primary control of certain types of cancer. He cites the Highland Park meeting of 1957, the proceedings of which I edited, in support of this statement. The purpose of my citation of the Fletcher article, however, was precisely that it furnished valid comparative data for the first time in a large enough series of patients. Since they were not available at the time of the Highland Park meeting, the Fletcher data must be regarded as superseding the negative statements that were made by a number of participants at Highland Park.

Both writers refer to the discrepancy between the previously published peak energy of 4 mvp and my reference to an energy of 6 mev for our medical linear accelerator at Stanford University. Radiologists ordinarily refer to conventional x-ray apparatus as being 200-kv. machines, even though only the peak energy of the beam, which is a small fraction of the total, actually fits this description. The linear accelerator is subject to changes in its operating efficiency from time to time. When our staff of physicists, headed by Dr. Mitchel Weissbluth, made the initial measurements, it appeared that the peak energy of the machine was in the vicinity of 4 mev. As indicated in the article by Ginzton and co-workers (*Stanford M. Bull.* **15**:123 [Aug.] 1957) the machine was designed for 6 mev. With appropriate tuning of its electronic components, it can be expected to operate with a peak energy at close to 6 mev. I judge that this point has been raised more for its nuisance value than through any "passion for accuracy."

Dr. Sisson's letter adds that the Fletcher data are not five-year survival rates, but this was explicitly stated in my article and is also stated by Fletcher. Sisson's second point, that adequate depth dose is not a limiting factor in present-day radiotherapy, is not true, and the argument that skin reaction is a useful and necessary clinical guide reflects a dangerous reliance on this visible biological response as a substitute for careful and precise dosimetry.

Dr. Macdonald's hope that I may be making some contribution to the education of the general radiologist misses the point completely. The difficulty does not lie in the quality of the product turned out by our residency training programs but rather in the fact that cancer, although a major public health problem, is paradoxically a relatively rare disease in the practice of the average physician. No matter how well trained he may have been in radiotherapy, the young radiologist doing general practice in radiology (a most useful and important occupation, which my comment was not intended to decry) will see but a handful of patients with cancers of all types and all stages. Perhaps five years will elapse in his practice between one patient with cancer of the floor of the mouth suitable for radium needle implantation and the next one suitable for the same treatment. Under these conditions, he cannot possibly remain even as well qualified in radiotherapy as he was at the conclusion of his residency. It is primarily for this reason that I urged the greater use of adequately staffed and well-equipped radiotherapy centers for the treatment of as many patients with potentially curable cancer as possible. I know many general radiologists who accept this view as firmly as I do and who confine their radiotherapy largely or exclusively to palliation and to patients with nonneoplastic problems, referring those with any chance for cure to centers where their chances can be maximized. This seems to reflect an admirably responsible conception of their role and can be expected to contribute, in the long run, to public esteem for the specialty of radiology.

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CLUSTER HEADACHES

To the Editor:—One becomes more than discouraged when reading such gems of "knowledge" about Harris's migraine or cluster headaches (also called Horton's headache or histamine headache) as the editorial in The Journal, Oct. 31, page 1224. One wonders also if the old professor was not right when he said, "There seems to be a preponderance of diarrhea of expression and a constipation of thought." Now we physicians are coyly introduced to a "new" treatment, consisting of regular ergotamine injections.

I personally have "cured" a patient with Horton's headache with histamine injections (according to Horton's technique), but when the headaches returned one year later they were equally well cured by vitamin injections, given in the same syringe, in increasing doses, at decreasing intervals of time.

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To the Editor:—My comment to Dr. Haffke's letter is as follows. Any physician of experience can cite an example of unexplained relief of a symptom by one or another drug or method. The "placebo effect," as it has been termed, must have been the usual means of relief of many and various symptoms prior to the introduction of specifics into medicine. There is reasonably general agreement, among those who have had much experience with cluster headache, that substances other than ergot preparations will not relieve the symptom by more than the percentage attributable to this "placebo effect," which investigators have determined to be as high as 40% (Batterman: *Yale J. Biol. & Med.* **18**:595 [July] 1946; Beecher: *Pharmacol. Rev.* **9**:59 [March] 1957; Wolf and Pinsky: *J. A. M. A.* **155**:339 [May 22] 1954). Cure of any of the many varieties of migraine is another matter.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Inhibition of Cholesterol Synthesis with the Use of MER-29. W. Oaks, P. Lisan and J. M. Moyer. A. M. A. Arch. Int. Med. 104:527-531 (Oct.) 1959 [Chicago].

The authors report on 41 patients with a serum cholesterol level of more than 250 mg. per 100 cc., who were treated with a proprietary preparation of triparanol (MER-29), a synthetic compound. Previous experiments on rats had shown that MER-29 inhibits cholesterol synthesis in the liver. Of the 41 patients, 11 received a dose of 250 mg. of the drug per day, 13 received 500 mg. per day, and 17 received 1,000 mg. per day. The over-all results in 36 patients who received the drug for 4 weeks or more showed a mean cholesterol depression of 35 mg. per 100 cc. after 1 week of therapy, which then progressed to a maximum of 58 mg. per 100 cc. by the 4th week. By virtue of its enzymatic inhibitory action on cholesterol synthesis in the liver, the drug thus produced a statistically significant depression in the serum cholesterol concentration of these patients. The drug was well tolerated in the dosage levels used and was relatively free from toxic side-effects. It is concluded that MER-29 is an effective drug for lowering the serum cholesterol level and warrants further investigation.

The Problem of Cardiac Hypertrophy During the Course of Coronary Disease. M. Castellano, F. Furno, G. Randone and A. Bigo. Minerva med. 50:2589-2594 (Aug. 25) 1959 (In Italian) [Turin, Italy].

The authors report on a study of cardiac hypertrophy in 100 normotensive patients with coronary disease, 41 of them with coronary insufficiency and 59 with coronary insufficiency and previous myocardial infarction. None of the patients presented, on clinical examinations and on laboratory tests, actual or previous factors, such as valvular disease or hypertension, which could have been responsible for the hypertrophy of the heart. The size of the heart in the 100 patients was measured by means of telecardiograms in the anterior, posterior, and lateral positions. The diameters of the heart were larger than normal in all instances. The percentage variation ranged from 4.1% for the basal diameter to 12.2% for the longitudinal diameter, and the volume of the heart had increased 21.1% in the patients with coronary insufficiency who had suffered no infarction. The percentage variation ranged from 5.5% for the basal diameter to 12.4% for the longitudinal diameter, and the volume of the heart had increased 22.8% in the patients with coronary disease who, in addition, had suffered myocardial infarction at least 4 months before the observation. The results show that the myocardial infarction did not cause an increase in the dimensions of the heart much greater than the increase observed in patients with only coronary insufficiency. The authors believe that the incidence of cardiac hypertrophy during the course of coronary disease is probably due to the hypertrophic action of the distention of the myocardial fibers, which follows hypotonus of the heart in case of insufficient blood supply.

Subendocardial Fibroelastosis in an Adult Woman. J. De L. Mignault, C. Goulet, F. Gagne and J. H. Laliberte. Canad. M. A. J. 81:483-486 (Sept. 15) 1959 [Toronto].

The case of a 48-year-old woman in whom subendocardial fibroelastosis was found at autopsy is reported. About 19 months before death the patient presented an influenza-like syndrome, including general malaise and a temperature of 103 F (39.4 C) which lasted 4 or 5 days. After a period of 10 months the patient developed progressive dyspnea, dry cough, orthopnea, and dyspnea even at rest, and lost 20 to 25 lb. (9.1 to 11.3 kg.) in body weight. On physical examination she appeared orthopneic and cyanosed. The jugular veins were distended, the heart appeared clinically enlarged, and a gallop rhythm was heard. The right lung base was dull and silent. The liver was tender and palpable 4 cm. below the costal margin, in the midclavicular line. No edema or ascites was noted. Chest radiography confirmed the presence of a right-sided hydrothorax. The heart was enlarged, with a cardiothoracic ratio of 18/27. A complete left bundle-branch block and signs of dilatation of the left atrium were noted on the electrocardiogram. Ordinary therapeutic means were used to control the congestive heart failure. Two consecutive thoracenteses produced, respectively, 800 and 650 cc. of clear, straw-colored, Rivalta-negative

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The place of publication of the periodical appears in brackets preceding each abstract.

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fluid. On cytological examination, multiple atypical cells, none of them, however, indicating malignancy, were noticed. Signs of thrombophlebitis of the right leg were noticed on the third day of hospitalization.

After a short period of some improvement the condition of the patient became progressively worse; in the end she developed severe bronchitis and died. On autopsy, the heart appeared markedly hypertrophied; the left ventricular endocardium, especially the septal wall, was white and smooth. A small red thrombus, 10 mm. in diameter, was attached to the papillary muscles of the right ventricle. The venae cavae and the coronary sinus were distended. A few yellow atheromatous plaques were present in the intima of the aorta. Microscopically, the endocardium of the left ventricle was thickened, fibrous, and rich in elastic fibers. Some pulmonary lesions, which were noticed, proved to be areas of infarction of different ages, most of them rather recent. The authors believe that in milder cases of subendocardial fibroelastosis a patient can remain asymptomatic for years, but once the first manifestations of congestive heart failure occur, the patient's condition deteriorates rapidly. Subendocardial fibroelastosis is to be suspected in any case of left ventricular failure of unknown etiology.

Pulmonary Tuberculosis in Patients with Congenital Heart Disease. A. Actis Dato, G. Bono and O. Cennamo. Minerva pediat. 11:841-853 (Sept. 8) 1959 (In Italian) [Turin, Italy].

Pulmonary tuberculous lesions were revealed in 8 patients, aged between 7 and 25 years, among 1,475 patients with congenital heart disease. The 8 patients had a diminished pulmonary blood flow. Six patients had the tetralogy of Fallot, 1 had a cardiac triad, and 1 had a single ventricle, stenosis of the pulmonary artery, and transposition of the large vessels. Six patients underwent cardiac surgery; in 5 the aorta or the subclavian and pulmonary arteries were surgically corrected, and in 1 pulmonary valvulotomy, with closure of the interatrial communication, was performed. The involved pulmonary lobe was resected in one patient. Three of the patients who were operated on died; the first died during the operation of ventricular fibrillation, the second died immediately after the operation of anoxic cerebral lesion, and the third died apparently of a severe toxemia on the third postoperative day. It seems that the latter death, however, could be attributed to the pulmonary rather than to the cardiac condition.

Pulmonary tuberculosis in patients with congenital heart disease can generally be treated as in patients without the heart condition. Pulmonary resection, if indicated, may be performed after, but not simultaneously with, the surgical correction of the cardiac disorder. Collapse therapy, if indicated, may also be performed after correction of the diminished pulmonary blood flow.

Chlorothiazide: A New Approach in the Treatment of Hypertension. D. Stuckey. M. J. Australia. 2:349-352 (Sept. 12) 1959 [Sydney].

Chlorothiazide, a diuretic agent, has been shown to be as effective by mouth as are organic mercurials given by injections. It has also been shown to potentiate the effects of numerous hypotensive agents, especially the ganglion-blocking drugs. The author reviews observations on 20 hypertensive patients, who constituted a consecutive series from hospital and private practice, the great majority of whom had been under personal observation and treatment with chlorothiazide for at least 6 months. Two patients died during the period of observation, one from a ruptured gangrenous appendix and the other from a second large myocardial infarction. Two patients had had a previous cerebral vascular accident. One patient was crippled from a severe burnt-out rheumatoid arthritis, and another had pulmonary emphysema. In 2 instances repeated attacks of urinary tract infection had occurred earlier in life, so that the hypertension of these patients was probably renal in origin. A family history of hypertension and vascular disease was noted in 3 patients.

With one exception, patients with diastolic pressures of 130 mm. Hg or more were admitted to hospital. A period of 4 to 7 days' observation, during which time control readings were taken, was followed by a similar period on chlorothiazide therapy alone before other hypotensive drugs were added. After the patient's discharge from hospital, further adjustment of drug dosage was almost always necessary. In the less severe cases all observations were made on an outpatient basis, and after an observation period of several weeks combined treatment with chlorothiazide and another drug was started. Apart from weight reduction in obese patients and advice against excessive salt intake, no manipulation of the diet was attempted.

On the experience in the present series, the conditions of most hypertensive patients with mean arterial pressures of less than 160 mm. Hg can be adequately controlled without ganglion-blocking agents, and these patients can be started at once on chlorothiazide combined with some other hypotensive drug. For patients with more severe hypertension and mean arterial pressures of 160 mm. Hg or more, ganglion-blocking drugs will almost always be necessary to achieve adequate control. In such cases it is wise to give chlorothiazide alone for about a week; then a ganglion-blocking drug is added, in small doses at first and gradually increased every few days. Addition of another hypotensive drug to the regimen may be necessary.

Clinical Experience With Chlorpropamide in the Treatment of Diabetes. G. G. Duncan. Diabetes 8:364-370 (Sept.-Oct.) 1959 [New York].

The author's study of the properties of chlorpropamide, involving 15 closely observed hospitalized patients with diabetes, indicates that this drug is a potent blood sugar reducing agent when given in doses as small as 0.25 to 0.5 Gm. per day. Moreover, after 1 Gm. of the drug has been given orally, its effect in lowering the blood sugar level becomes apparent between 2 and 4 hours after the administration, and this effect extends beyond 24 hours. After a 5-day test period, the drug is withdrawn, and its hypoglycemic effect gradually disappears over a period of 3 to 5 days.

In a study extending over 3 test periods and 6 months' follow-up, chlorpropamide served, with suitable dietary measures, to control the disease in 10 of the 15 hospitalized patients having "adult-acquired" diabetes. In no instance was it necessary to discontinue the therapy because of side-effects, although one patient had a transitory macular skin eruption. No significant hematological, renal, or hepatic disorders attributable to this therapy were observed in these patients. The detection of acetonuria in increasing amounts after a reduction in the amount of insulin given served as a reliable guide in detecting those patients in whom a satisfactory response with chlorpropamide would not be obtained, whereas in patients in whom no acetonuria occurred, there would be a satisfactory response to chlorpropamide therapy.

In a study involving 32 outpatients reported by other investigators, chlorpropamide therapy reduced the blood sugar level more than 20% in each of 25 patients. All these patients were over 40 years of age and had had diabetes for an average of 7 years. Hypoglycemic reactions were not common in these patients, but they occurred more in those taking chlorpropamide than in those taking tolbutamide.

These studies on the treatment of diabetic subjects with sulfonylurea compounds indicate that at least two-thirds of the adult overweight patients respond to such therapy and that chlorpropamide is a more potent blood sugar reducing agent than is tolbutamide. However, since most of these patients respond to dietary treatment alone, oral drug therapy is a needless, although occasionally effective, supplementary measure. Likewise, patients who are underweight or of normal weight and who have a stable form of diabetes but need drug therapy may respond favorably to insulin or a sulfonylurea, as indeed more than 50% do. But it is in this group that the favorable effect of such a sulfonylurea as tolbutamide is most frequently temporary. It would appear that chlorpropamide and other sulfonylureas, though quite effective in controlling diabetes in selected cases, are still on trial. Surveillance under close scrutiny for long periods is still necessary to prove the harmlessness of the sulfonylurea compounds. Also, the possibility that such agents might receive widespread adoption as a substitute for appropriate dietary measures must be guarded against.

Polycythemia in Renal Carcinoma. G. Omland. Acta med. scandinav. 164:451-454 (no. 6) 1959 (In English) [Stockholm].

The author reports on a 63-year-old woman who has been under observation since 1949 when an orange-sized tumor was detected in her right kidney. She was also found to suffer from polycythemia. After removal of the carcinoma of the kidney, the polycythemia regressed, and the patient was well for several years. In 1953 pulmonary symptoms developed, highly suggestive of metastases, and the polycythemia reappeared. Intensive roentgen-ray treatment of the tumor of the lungs temporarily stopped its growth and also brought about a regression of the polycythemia, after which the patient was fairly well for approximately 2 years. Then a tumor of the esophagus appeared, which was histologically proved to be a metastasis from the carcinoma of the kidney, and the polycythemia again reappeared. Three remissions of polycythemia have occurred in this patient in the course of 9 years. A causal relationship between carcinoma and polycythemia may have existed in this patient.

Nondiagnostic Bone Marrow in Leukemia. H. W. Fisher and W. H. Civin. Hawaii M. J. 19:37-43 (Sept.-Oct.) 1959 [Honolulu].

The authors report on 5 women, between the ages of 30 and 70 years, and a 71-year-old man who had symptoms of leukemia for periods varying from 6 weeks to 2½ years before bone marrow smears revealed the characteristic hyperplasia. The cases of these 6 patients were among those of 43 patients who were treated for leukemia at the Queen's Hospital in Honolulu within the last 8 years. Thus, almost one case in 7 could not be diagnosed initially as leukemia, although hematological studies were performed. In the other 37 patients, the diagnosis was made without significant difficulty at the start of clinical illness. All 6 patients from whom nondiagnostic bone marrow specimens were obtained had acute leukemia: 1 had lymphocytic leukemia; 2, granulocytic leukemia; 2, stem-cell leukemia; and 1, monocytic leukemia. Each of the 6 patients had an initial anemia more or less refractory to therapy. There was leukopenia in one of the patients with lymphocytic leukemia and in the 2 patients with stem-cell leukemia. There was leukocytosis in the patient with monocytic leukemia. Thrombocytopenia was present in 4 patients—1 with granulocytic, 1 with monocytic, and 2 with stem-cell leukemia. The bone marrow was initially hypoplastic in the 2 patients with stem-cell leukemia and in one of the patients with granulocytic leukemia. The marrow was initially unremarkable in the other 3 patients. There was initial enlargement of lymph nodes, liver, and spleen in one of the patients with stem-cell leukemia, and of liver and spleen alone in the other patient with stem-cell leukemia.

In the preleukemic phase of leukemia the bone marrow may be normal, it may show only minor and nonspecific changes, or it may be hypocellular as it was in 3 of the 6 patients. Refractory anemia is frequently an outstanding feature. Enlargement of lymph nodes, liver, or spleen is inconstant. It is suggested that specimens of nondiagnostic bone marrow be obtained early in leukemia, because (1) early changes may be localized and missed by marrow aspirations, (2) the early changes may be extramedullary and not present in the marrow at all, or (3) in certain patients with leukemia the marrow may be hypocellular before it becomes hyperplastic.

Clinical Experiences with Determination of Serum Enzymes. J. Beyreder and H. Rettenbacher-Däubner. Wien. klin. Wchnschr. 71:686-692 (Sept. 4) 1959 (In German) [Vienna].

The authors determined the concentration of serum glutamic oxalacetic transaminase (SGO-T), serum glutamic pyruvic transaminase (SGP-T), and serum lactic acid dehydrogenase (LDH) in 538 patients who were admitted to the medical department of the Empress Elizabeth Hospital in Vienna. In many of these patients repeated enzyme determinations were made, and the results were recorded graphically in an attempt to ascertain the changes in the enzyme concentration in the serum in the course of their diseases and under the influence of therapy. A considerable number of patients had diseases of the liver, and, in addition, there were many with diseases of the blood. The SGP-T and the SGO-T activities showed a synonymous behavior, particularly in patients with acute infectious hepatitis in whom the highest enzyme values were found. The SGO-T/SGP-T quotient mentioned by other workers is normally above 1.0 and decreases to below 0.7 in patients with acute hepatitis. This behavior does not, however, present a definite differential-diagnostic indication, since this quotient also has been found to be below 1.0 in about 70% of the patients with obstructive jaundice. In some patients with cirrhosis of the liver, and particularly in those with chronic cholangiolitic processes, the SGO-T concentration showed a greater increase than the SGP-T concentration. The determination of the SGO-T or the SGP-T concentration is of great value for the diagnosis and differential diagnosis in patients with acute hepatitis and for the evaluation of the activity of the disease process in patients with chronic hepatitis and in certain phases of posthepatocirrhosis of the liver. In patients with hepatitis, cortisone and prednisolone therapy also seems to influence the derailment of the enzymes, and it seems to lead to a reduction of the increased enzyme level in the serum.

The laparoscopic findings and the results of biopsy showed frequently satisfactory agreement between the extent of the enzyme derailment and the severity and activity of the inflammatory and degenerative changes in the liver of patients with hepatitis; in addition, this agreement was also seen in some of the patients with cirrhosis of the liver, and particularly in those with chronic cholangiolitic processes. Frequently the enzyme tests were superior to most of the other liver function tests which were employed for the evaluation of the patients.

Of the patients with diseases of the liver, the serum LDH values have offered practical aid only in the diagnosis of metastases of the liver. In such cases, the serum LDH concentration may be increased to 7,000 or 8,000 units, in contrast to only slight increases in SGO-T and SGP-T concentrations. In doubtful cases, the determination of the LDH concentration may thus be a valuable diagnostic aid, while it is of no clinical significance in other diseases of the liver. The significant brief increase in SGO-T and SGP-T values in patients with recent myocardial infarction has a well-known diagnostic value, and this excellent diagnostic value has been confirmed in patients in whom myocardial infarction is suspected. In other cardiac diseases, perhaps with the exception of myocarditis, the enzyme determinations do not play any significant role.

A notable, and occasionally even enormous, increase in serum LDH values was observed regularly in untreated patients with pernicious anemia, in whom this enzyme determination offers aid in diagnosis. The serum LDH concentration was restored to normal within 10 to 14 days of vitamin B_{12} therapy. In patients with hemolytic anemia of various origin, the serum LDH concentration was often increased, and there was a certain parallelism with the intensiveness of the hemolysis.

SURGERY

Ventriculo-Auriculostomy in Treatment of Hydrocephalus. F. M. Anderson. J. Neurosurg. 16:551-557 (Sept.) 1959 [Springfield, Ill.].

The results of the surgical treatment of 36 patients with hydrocephalus were surveyed within 1 to 24 months after the initial operation. There were 20 males and 16 females in the series, with ages that varied from 4 weeks to 30 years. The preoperative diagnosis indicated congenital internal hydrocephalus in 23 patients, hydrocephalus caused by meningitis or ventriculitis in 8, tumor of the brain stem in 2, chronic intracranial hypertension of undetermined cause in one, and unresectable cerebellar tumor in one. The ventriculoauriculostomy procedure used was the technique originated by Pudenz, and consisted of a shunt between the right lateral cerebral ventricle and the blood stream in the right auricle of the heart, by means of a small Silicone rubber tube having a simple undirectional slit valve at the intracardiac end.

Twenty-three patients were alive at the time of this survey. In 17 there were no signs of recurrent intracranial hypertension. Their postoperative course had been uneventful; they had resumed normal feeding schedules quickly, and had left the hospital 8 days after the operation. The circumference of the head decreased slightly in a few; in others the head had grown slowly, and the head-chest disproportion had decreased. In 5 of the 23 survivors it was neceessary to revise the shunt surgically one or more times. In 2 of these patients the ventriculoauriculostomy was abandoned after several revisions, and an arachnoidureterostomy was performed. One survivor progressed satisfactorily for 2 months, then could no longer be followed up.

The author lists some unfavorable features of the procedure and recommends certain corrective measures: 1. Revision of the original operation will be required in a certain number of cases, due to blockage of the shunting tube and occlusion of the valve by adherence of its slit margins. Coating the valve slit with molybdenum sulfide greatly diminishes the probability of blockage. 2. Potential problems are created by the growth of infants and young children, for the elongation of the vena cava and the jugular vein displaces the valve upward, causing stenosis around the tube and blocking the shunt. It is advised that the tubing be tied only at the point of entrance into the vein and a 10-cm.-long tube be placed into the ventricle. 3. Because diverting of cerebrospinal fluid into the blood stream or subarachnoid spaces may disseminate an infection, this procedure should not be applied until at least 2 months after the bacteriological cure of meningitis or ventriculitis. In the author's opinion, the inherent advantages of the technique far outweigh its unfavorable features. It is not a difficult technique, although painstaking. The key structures utilized for the shunt are of good size and readily cannulated. The procedure is suitable for hydrocephalus of any variety. Because excess cerebrospinal fluid is diverted into the blood stream, there are no postoperative difficulties with loss of water or electrolytes, or accumulation of fluid in body cavities. It is concluded that the ventriculoauriculostomy is a surgical procedure of considerable merit, deserving of continued trial.

Immediate and Late Results of Surgery in Cases of Saccular Intracranial Aneurysms. J. G. Hamilton and M. A. Falconer. J. Neurosurg. 16:514-541 (Sept.) 1959 [Springfield, Ill.].

A follow-up study of the survivors among 2 series of patients operated on for subarachnoid hemorrhage caused by saccular intracranial aneurysm is reported. The first series comprised 50 patients who were operated on in New Zealand between 1946 and 1950; the second series comprised 62 patients who were operated on in the Guy's-Maudsley neurosurgical unit in London between 1950 and 1955. Of these 112 patients, 109 had aneurysm complicated by intracranial hemorrhage, as demonstrated by 118 arteriographies. The surgical approach and technique varied enormously according to the type and localization of the aneurysm. There were 6 categories of lesions: 1. Aneurysm of the internal carotid artery at the posterior communicating artery. Of the 41 patients in this group, 38 were operated on by either carotid ligation under local anesthesia or craniotomy under general anesthesia, or by a combination of these methods. One patient collapsed during arteriography and died within a few hours, and 2 patients, who never had frank subarachnoid hemorrhage, underwent ligation of a common carotid artery in stages, followed by ligation of the external carotid artery. 2. Aneurysm at the carotid bifurcation (7 patients). Two patients had carotid ligation as their only treatment; 5 underwent craniotomy, including 2 muscle wrappings. 3. Aneurysm of the anerior cerebral artery (34 patients). These patients were treated in a variety of ways. As the results of carotid ligation were unsatisfactory, most of them underwent intracranial operation with either clipping of the arterial neck or wrapping with muscle. 4. Aneurysm of the middle cerebral artery (17 patients). One patient was operated on by a direct approach, and most of the others were treated by either carotid ligation or primary intracranial attack, or by a combined operation. 5. Aneurysm of the basilar artery and its branches (3 patients). Treatment of these patients was by ligation of one vertebral artery in the neck. 6. Multiple aneurysms. The treatment was dictated by the situation of the lesion and the severity of the symptoms. Bilateral carotid angiography was the rule, and there was no hesitation in attacking the lesions on both sides.

The 93 survivors (86% of the combined series) were followed up for periods ranging from 2 to 9 years. There was recurrence of bleeding in 8 patients, resulting in death of 4 of them. In at least 2 of the fatal cases, the recurrent bleeding did not come from the aneurysm operated on, but from a second unsuspected aneurysm. Of the 85 patients who survived the follow-up study, 71 (65% of the total number) made excellent recovery and resumed their former activities with little or no disability or inconvenience. The authors emphasize the importance of the timing and management of arteriography. It is their impression that early surgical treatment does not improve the chances of survival, for approximately 30% of the patients with subarachnoid hemorrhage die within 2 or 3 days after the bleeding, whether the treatment is conservative or surgical. If arteriography can be deferred until a week after the hemorrhage and then be followed by prompt operation, most of the deaths from subsequent recurrent bleeding can be avoided; few complications occur after the arteriography, and the prospects for the patients can be greatly improved.

Fracture of the Cervical Spine in Patients with Rheumatoid Arthritis. L. J. Lemmen and P. G. Lain. J. Neurosurg. 16:542-550 (Sept.) 1959 [Springfield, Ill.].

When fractured, the ankylosed spine breaks like a long bone and constitutes a difficult problem, especially since this fracture usually occurs in older or chronically ill patients. Rapid bony healing at the site of the fracture may not take place in a cervical spine with even minimal signs of rheumatoid arthritis. Three cases are described as illustrations of the therapeutic problems presented by these fractures. The first patient was a 51-year-old man who had suffered from typical ankylosing arthritis for 24 years. He fell backward from a truck, striking his shoulders. Three months later he felt weakness of the extremities and difficulty in walking. He was placed on a Foster frame, and traction with 20 lb. of weight was applied to Crutchfield tongs. Twelve hours later he was operated on under general anesthesia, and tracheal intubation was attempted. As considerable bleeding and cyanosis occurred, tracheotomy was performed. Twelve hours after the operation, as the traction was reduced to 10 lb., tetraplegia and urinary retention developed. Decompressive laminectomy was performed 4 days later. Three months later acute respiratory difficulty developed, and the patient died suddenly. The second patient, a 63-year-old man, was admitted to the hospital with symptoms of urinary retention and mental confusion. Roentgenograms showed extensive rheumatoid spondylitis of the cervical and the thoracic spine. The patient was placed on a Foster frame, and traction with 4 lb. of weight was applied to Crutchfield tongs. Roentgenograms taken 24 hours later showed hyperextension of the upper part of the cervical spine. The patient died suddenly when turned from face-down to face-up position. Autopsy revealed central hematomyelia of the spinal cord at the level of the fracture. The third patient, a 60-year-old man, had suffered from a "frozen spine" for 27 years. He fell out of bed and struck his head. Roentgenographic examination revealed a fracture of the ankylosed cervical spine between the 6th and 7th vertebrae, extending through the bodies and neural arches. The upper cervical spine was displaced anteriorly; the neural arches were displaced and locked. The patient was placed flat on his back with his head supported on a pillow in its usual position of forward flexion; later he was fitted with a padded cervical collar and an adjustable cervical collar. No signs of involvement of the spinal cord or of cervical nerve roots appeared during the treatment. Ten weeks later solid union of the cervical spine in its displaced position was demonstrated by roentgenograms.

The prognosis and modes of therapy depend on the degree of vertebral displacement, concurrent spinal cord injury, and general condition of the patient. Absence of neurological signs permits conservative and minimal therapy, even with considerable vertebral displacement, as illustrated with the third patient. Neurological symptoms are indication for reduction of the fracture by traction. In the first patient, a 20-lb. traction was permitted prior to the anesthesia. Relaxation of the cervical muscles with general anesthesia and the mode of cervical traction of the Foster frame were considered responsible for the development of increased neurological deficits. The effect of traction in cases of locking in hyperextension was revealed by the roentgenograms taken of the second patient, in whom it resulted in hyperextension of the cephalad portion of the ankylosed spine and increase of the bony deformity. The authors advise that preliminary tracheotomy under local anesthesia should be performed in order to provide a satisfactory airway for general anesthesia during open reduction. Delay in applying skeletal traction seems advisable until open exposure has been accomplished under general anesthesia.

Blood Donor Problems with the Use of Heart-Lung Bypass Machine. J. J. van Rood and J. van der Sluys Veer. Thoraxchirurgie 7:131-139 (Aug.) 1959 (In German) [Stuttgart, Germany].

When operations with extracorporeal circulation are planned at a clinic, an increase of about 25% in respect to provision of blood must be taken into account. The authors, therefore, advise, as early as possible, blood bank and blood transfusion service on the operations planned. The blood must be collected on the day of the operation in Silicone-coated vacuum bottles containing heparin and human protein. Crossmatching of all stored blood with that of the patient is indispensable and must be performed with the aid of sodium chloride and the indirect Coombs test. There is no general agreement on the indispensability of interdonor crossmatching. The so-called mixed serum crossmatching can be used as an intermediate solution.

Experimental Study of the Increase of Coronary Flow by Constriction of the Ascending Aorta in the Treatment of Coronary Insufficiency. B. C. Villagrana, R. Buzzi and M. E. De Bakey. Arch. Inst. cardiol. México 29:421-439 (July-Aug.) 1959 (In Spanish) [Mexico, D. F.].

The effect on the coronary flow of an artificial aortic resistance, induced by a moderate constriction at the level of the ascending segment, was experimentally studied in 5 groups of dogs. Four groups were composed of 10 dogs each, and one group was composed of 5. The aortic constriction was applied in varying degrees with use of an umbilical tape. Blood for the quantitative evaluation of the coronary flow was obtained in 2 ways: outgoing blood collected through a catheter inserted into the coronary sinus, and blood collected from the right ventricle after derivation of the caval circulation into the pulmonary artery through a pump of constant flow. The degree of constriction was evaluated by measuring the blood pressure in the left ventricle and the aorta, proximal and distal to the place of constriction.

The dogs in the first group were killed after the experiment. Those in the second group underwent a second operation within 5 to 90 days after the first one, in order to recatheterize the coronary sinus and measure the blood pressure. The animals were then killed for autopsy. The third group of dogs underwent simultaneous constriction of the ascending aorta and ligation of the descending aorta near the brachycephalic trunk. Postoperative blood pressure varied between 15 and 25 mm. Hg. One dog died within 24 hours of the operation, another 3 days later, and still another 15 days later. The surviving animals were reoperated on at intervals of 20 to 100 days after the operation, and were killed after a new evaluation of the blood pressure and of the flow in the coronary sinus. In the fourth group, the anterior descending branch of the left coronary artery was ligated. Six dogs died after the operation. The surviving animals were reoperated on between 15 and 19 days later; at this second operation their blood pressure gradient was 5 to 20 mm. Hg. The dogs were killed 45 days later, after new measurement of the coronary flow and of the blood pressure. In the dogs of the fifth group, the blood was diverted from the subclavian into the coronary arteries by means of a pump of constant flow. The pressure in the descending aorta was maintained constant by a heart-lung machine.

In the first and fifth groups of dogs, the effects of the compression of the aorta showed that a moderate constriction of the ascending aorta causes a gradient of blood pressure not higher than 30 mm. Hg. It increases the coronary flow by 20 to 60%, not at the expense of cardiac output. The effects observed in the other experimental groups showed that the increase in the coronary flow is maintained if the pressure gradient is kept constant. The over-all results suggest that the repercussion of the artificial stenosis on the cardiac function is minimal and well tolerated, and that the increase in the coronary flow, supposedly distributed through intercoronary anastomoses, protects the heart against the effects of the ligation of a coronary branch. The authors believe that the use of such a simple surgical procedure as a moderate constriction of the ascending aorta is capable of releasing the coronary flow from ischemia and can be an effective treatment of coronary insufficiency.

Late Results of Operations for Mitral Stenosis. V. W. Schaub and W. Hager. Deutsche med. Wchnschr. 84:1675-1679 (Sept. 11) 1959 (In German) [Stuttgart, Germany].

To ascertain the late results of mitral valvotomy, the authors invited 178 patients, in whom more than 3 years had elapsed since operation, to return for a clinical checkup. In all, 116 patients complied with this request; 14 others were known to have died in the meantime. Some other patients described their condition in a letter, but these were not included in the report. The 130 patients evaluated included 102 women and 28 men; the time elapsed since operation ranged from 3 to 8 years. Eighty-five patients had only stenosis of the mitral valve, whereas the other 45 had some mitral insufficiency in addition to the predominating stenosis. In addition to the mitral valve lesions, 4 patients (2 in each of the 2 groups) had aortic stenosis; furthermore, of the first group 2 had aortic insufficiency, and 2 of the second group had tricuspid insufficiency. While some of the 14 deaths resulted from cardiac insufficiency, one patient in whom the valvotomy had been successful died from an accident, and in other cases the cause of death was not stated.

Of the 116 patients who were reexamined, 33 had obtained excellent and 53 good results, 15 others had experienced moderate improvement, and the condition of 15 was practically the same as before the operation. Incomplete valvotomy, because of unfavorable anatomic conditions or extreme calcification, and recurrent stenosis were the main causes of the unsatisfactory results. In the other patients with poor results there was a discrepancy between the objective findings (severity of the stenosis) and the subjective complaints. Possible contributing causes were secondary pulmonary arteriosclerosis with pulmonary hypertension, additional valvular defects, or "bronchiospastic emphysema."

The excellent or good results were reflected in the behavior of the electrocardiogram, which showed a leftward rotation of the greatest instantaneous QRS vector and reversal toward normal of the ST-T segment. Roentgenologic examination of the greatly improved patients revealed a decrease in the size of the left atrium. An enlargement of the heart toward the left was found so often in all groups of patients that it is of no importance in the evaluation of the operative results. This leftward widening can indicate an enlargement of the left as well as of the right ventricle. Patients who obtained poor results from surgery showed, in addition to left ventricular enlargement, dilatation on the right side of the heart. A decrease in the size of the right atrium was never observed in these patients.

Anatomic and Clinical Study of Amputation: 57 Cases of Amputation of the Extremities. P. H. Benavides de Anda, G. M. Alvarado and E. S. Dávila. Arch. Inst. cardiol. México 29:486-503 (July-Aug.) 1959 (In Spanish) [Mexico D. F.].

The records of 57 patients who underwent amputation of an extremity at the Instituto Nacional de Cardiología in Mexico during 1945-1958 are analyzed. There were 4 groups of patients. Group 1 comprised 28 patients with atherosclerosis; group 2, 18 patients with embolism; group 3, 7 patients with Buerger's disease; and group 4, 4 patients for whom a diagnosis had not been established. Complicating diseases in group 1 were diabetes in 11 patients, arterial hypertension in 6, and atherosclerotic cardiopathy in 17. The average interval between the initial symptoms of arterial insufficiency (intermittent claudication) and the amputation was 25 months. Treatment previous to the amputation had consisted in the administration of anticoagulants to 9 patients, sympathectomy in 5, femoral arteriectomy in 2, and femoral graft in one. The gangrene was ischemic only in 17 patients, and in 12 there was secondary infection. The 28 patients with atherosclerosis underwent 29 amputations; the immediate mortality was 21.4% (6 patients).

The 18 patients with embolism underwent 20 amputations for gangrene. The thrombosis was caused by rheumatic heart disease in 7 patients, by recent myocardial infarction in 5, and by angiosclerotic cardiopathy in 6. The average time interval between the occurrence of the embolism and the onset of trophic disturbances was 8 days. The average interval between the onset of embolism and the amputation was 19 days. The gangrene in these patients was of the ischemic type, with secondary infection in one patient. Seven patients died in the hospital, which means an immediate mortality of 35%. The 7 patients with Buerger's disease underwent 8 amputations. All 7 had undergone previous sympathectomy; there had also been arteriectomy in 3 patients and amputation of toes or fingers in 3. Two patients died of ascending thrombosis of the abdominal aorta. The 4 patients for whom a diagnosis had not been established were found to have nonspecific angiitis (2 patients), Leriche's syndrome (1 patient), and essential arterial hypertension (1 patient). One patient had postoperative migrating phlebitis and died 3 months after the operation. The authors recommend early operation for the patients with embolism, whereas in those with atherosclerosis amputation should be a last resource to save the patient's life.

PEDIATRICS

A Syndrome Featuring Defects of the Heart, Sternum, Diaphragm, and Anterior Abdominal Wall. I. H. Crittenden, F. H. Adams and D. G. Mulder. Circulation 20:396-404 (Sept.) 1959 [New York].

Three young children with congenital defects involving the heart, diaphragm, lower sternum, and anterior abdominal wall were recently studied at the University of California at Los Angeles. The features that characterized these patients were (1) malrotation of the heart with dextroposition, (2) intracardiac anomalies including ventricular septal defect, (3) deficient lower sternum, (4) anterior diaphragmatic defect, and (5) midline abdominal defect with diastasis recti and umbilical hernia. The midline deficiency permitted cardiac impulses to be seen and palpated in the epigastrium. The rotational position of the heart was demonstrated in each by selective angiography and electrocardiography. One child was operated on, and complete surgical repair of the defects, including amputation of a diverticulum from the left ventricle, was successful.

A review of the literature revealed that cases resembling the 3 described had been classed as a rare subgroup of ectopia cordis. This is probably an erroneous classification, and the authors feel that these patients should be considered as having a distinct syndrome. They suggest that the basic defect in the 3 patients was a failure of the mesoderm of the body wall to complete its migration to meet and fuse solidly in the ventral midline. This would account for the failure to fuse of the scleratome (cleft sternum and xiphoid process) and of the myotome (diastasis recti). This general failure also explains the presence of omphalocele, or umbilical hernia. The positional relationship of the heart suggests embryonic arrest with failure of complete rotation and bending to the left. A common gestational time can be presumed for the occurrence of the defects described, but no causative factor can be explained other than failure of the body wall mesoderm of complete migration and fusion in the ventral midline.

One can expect to find variation in cases of this type. Whether the same basic pathogenesis, differing only in degree, is responsible for mere dextroversion of the heart in one case and complete ectopia cordis in another is conjecture. Suffice it to say that the 3 cases reported are sufficiently distinct to be considered a syndrome.

Exanthem Associated with ECHO Virus Type 18 Viremia. D. N. Medearis Jr. and R. A. Kramer. J. Pediat. 55:367-373 (Sept.) 1959 [St. Louis].

Enteric cytopathogenic human orphan (ECHO) virus, type 18, was first isolated by Ramos-Alvarez during investigations of summer diarrhea. Since then, it has been shown to be etiologically responsible for diarrhea in infancy. Until very recently the virus had been recovered only from stool specimens. In virologic studies on the 3-week-old female infant whose case is presented, the virus was isolated from the blood, and it seems probable that the febrile exanthematous illness of this infant was caused by the recovered ECHO virus, type 18, or a closely related variant. Cytopathogenic viral agents recovered from the patient's blood, throat, and rectum were neutralized by ECHO 18 antiserum. During convalescence a significant (8-fold) rise in titer of serum neutralizing antibody was detected against the virus isolated. Whether the exanthem was caused by this concurrent viral infection cannot, however, be absolutely determined. The patient had received acetaminophen and oxytetracycline prior to the appearance of the rash. Both medications, or chemically very similar ones, have been associated with, and thus presumably have been the cause of, morbilliform skin eruptions. The clinical features of such rashes are not sufficiently characteristic to permit an etiological diagnosis. An 18-month-old sibling of the infant had a similar exanthematous illness, but he was not studied. Although the rash may have been due to acetaminophen or oxytetracycline, this is probably the first reported case of exanthem associated with ECHO virus, type 18. It is the first reported isolation of this virus from the blood. Definition of this disease must await additional observations.

Effects of Early Ambulation on the Course of Nephritis in Children. W. W. McCrory, D. S. Fleisher and W. B. Sohn. Pediatrics 24:395-399 (Sept) 1959 [Springfield, Ill.].

The course of convalescence from acute nephritis in 35 children, admitted to the Children's Hospital of Philadelphia and allowed early resumption of physical activity, was followed for at least 2 years. There were 27 boys and 8 girls in this group; their ages ranged from 2½ years to 12 years and 10 months. All the patients were kept in bed during the acute stage of nephritis, but were allowed to resume physical activity gradually, as soon as the acute symptoms had subsided. They were engaged in normal daily activity, including attendance at school, by 2 months at the latest after the onset of acute nephritis. All of them received penicillin in therapeutic doses during the first 7 to 10 days after the diagnosis of nephritis had been established. During the course of the follow-up study they also received a daily oral dose of 300,000 units of benzathine penicillin G, as a prophylactic treatment, until a normal Addis count of the urinary sediment was obtained. After discharge from the hospital the patients were seen at 2-week to one-month intervals for an examination which included checking on weight, measurement of blood pressure, and ordinary urinalysis.

Most of the patients had some degree of proteinuria and hematuria at the time of resumption of full physical activity. Although these abnormal urinary findings took a variable period of time to disappear, the majority of the patients had normal ordinary urinalysis at the end of 9 months from the onset of the disease. At the end of 2 years of follow-up observation, 34 of the 35 children studied had completely recovered, with no adverse signs or symptoms in association with early ambulation. Although the number of cases studied is too small for any statistical conclusion, the results obtained in this group are comparable to those obtained with any other therapeutic regimen. The value or necessity of continuing bed rest after the symptoms and signs of acute glomerulonephritis have subsided is considered unsubstantiated.

Relation of Duration of Bed Rest in Acute Rheumatic Fever to Heart Disease Present 2 to 14 Years Later. B. L. Lendrum, A. J. Simon and I. Mack. Pediatrics 24:389-394 (Sept.) 1959 [Springfield, Ill.].

A long-term study of the medical management of acute rheumatic fever was initiated at Herrick House in Bartlett, Ill., in 1946, when this former summer residence was converted into a year-round convalescent home for children suffering from rheumatic fever. Of the 500 children examined, 360, for whom there was an established diagnosis of rheumatic fever without association with any other type of disease, were followed up for a period of 2 to 14 years. Two hundred sixty-nine children who had been sent to Herrick House immediately after the disappearance of clinical evidences of rheumatic fever consituted the experimental group. The other 91 children, who were admitted to Herrick House as nonconvalescents, constituted the control group. They had been subjected to prolonged periods of bed rest and had been severely restricted by their parents or physicians to the point of becoming "cardiac cripples." Although this group had not been medically handled in a uniform manner, it was considered a valid control, because it was comparable to the experimental group in the quality of medical care received after leaving Herrick House, in the use of antistreptococcic prophylaxis, in the incidence of recurrences, chronic myocarditis, and subacute bacterial endocarditis, and in age distribution and number of years in the follow-up study.

The children in the experimental group followed a program of rapid rehabilitation, with an initial short period of bed rest during which they were studied for clinical manifestations of rheumatic activity. If certain physical and laboratory findings approached the normal limits, the patients were allowed increased activity, going gradually from stage 0 (bathroom privileges and mild sedentary activities only) to stage 5 (essentially unlimited activity, excluding strenuous or competitive effort). Most children advanced through these stages within 2 to 5 months. The average duration of stay at Herrick House was 3 months. In order to evaluate the results of the shortened bed-rest treatment, an arbitrary scoring system was developed on the basis of 3 types of change: (1) significant changes in murmurs on auscultation; (2) significant changes in heart size, as observed by fluoroscopy and on teleorentgenograms; and (3) significant changes in blood pressure caused by aortic insufficiency.

The cardiac status of the patients at the final follow-up examination was compared with the initial findings at the time of admission to Herrick House. In the experimental group, this status was better in 39 patients (14%), unchanged in 161 (60%), and worse in 69 (26%). In the control group, it was better in 11 patients (12%), unchanged in 43 (47%), and worse in 37 (41%). Excluding the patients who had suffered recurrences, subacute bacterial endocarditis, and chronic myocarditis, these percentages were: better clinical status in 18%, unchanged in 69%, and worse in 12% of the experimental group; better in 19%, unchanged in 56%, and worse in 25% of the control group. The findings support the contention that prolonged bed rest and restriction of activity after an acute attack of rheumatic fever are not necessary for optimal healing of the injured heart, and that early return to normal activity will avoid economic burden and psychological damage.

Duodenal Ulcers in Children with Notes on Their Etiology. J. O. Lafferty. Radiology 73:374-378 (Sept.) 1959 [Syracuse, N. Y.].

Since 1949 the author has made the diagnosis of duodenal ulcer 15 times in 92 children, ranging in age from 2 to 15 years, who had been referred for gastrointestinal studies. The symptoms of which these children complained are not at all those of the "typical" adult ulcer patient. Hunger pain and food relief are rare. Most often there is generalized abdominal pain, sometimes with vomiting, the latter recurring regularly at a particular time of day, which differs with the individual patient. Occasionally there will be bleeding. As the child grows older, the symptoms become more typically adult. Some gastroenterologists feel that a certain number of their adult ulcer patients had ulcers as children. It is true that older persons with well-developed ulcers and scarred caps, on questioning, are often found to have been subject to stomach-aches in their childhood years, or to have been characterized as "a child with a weak stomach."

The diagnosis of duodenal ulcers must be made radiographically, and the technique is similar to that used in adults. The treatment of children with ulcers is similar to that of adults—a bland diet with frequent feedings, mild sedation, antacids, and reassurance. Psychiatric help for the child and his parents is often of value in resolving an underlying conflict. Many of these children have deep-seated psychiatric problems, and help in these will do much to bring about improvement. Results of nonsurgical treatment are good. None of the patients seen by the author have required surgical treatment.

Empyema in Infants and Children as a Clinical Problem. T. M. Campbell Jr., M. E. Jenkins and R. B. Scott. J. Nat. M. A. 51:344-349 (Sept.) 1959 [New York].

With the recent increase in staphylococcic pneumonia, empyema has again emerged as an important clinical problem. This communication is concerned with 8 infants and children with empyema treated on the pediatric service of the Freedmen's Hospital, Washington, D. C., over a 2-year period (1957-1959). Staphylococcus pyogenes var. aureus was isolated in 7 patients and was a probable causative organism in the remaining case. The clinical histories are presented. All but 2 of the patients were less than 6 months old. The presenting symptoms varied, but cough and rapid respiration were present in all 8 patients. In the smaller infants coughing was less marked than in the older ones. Symptomatology, in general, tended to be less specific in the newborn and early infancy periods.

Typically, the cough of empyema is one of increased intrathoracic pressure, which is characteristically dry, hacking, and nonproductive, and is exaggerated by anything that causes a deep inspiration. Fever and respiratory distress are frequently seen. Severely affected infants may suddenly exhibit prostration, cyanosis, and even shock. Six of the infants had one or more emergency episodes of severe respiratory distress, and required almost constant vigilance during the first 48 to 72 hours of hospitalization. The outstanding roentgenographic finding in each of the 8 cases was evidence of pleural effusion, with the involved hemithorax presenting a fairly uniform, homogeneous opacification. Pyopneumothorax was observed in 3 of the 8 patients.

Although antibiotic therapy should be directed by sensitivity studies, treatment cannot always be delayed until these are completed. In nonhospital-acquired staphylococcic infections, high therapeutic dosages of penicillin may be employed until sensitivity studies are completed, after which penicillin therapy can be continued, or changed to another drug as indicated. Often therapy must be continued for many weeks, even months. Therefore, frequent cultures and sensitivity studies are necessary to detect the persistence of organisms and possible acquired antibiotic resistance. The authors feel that in nosocomial staphylococcic infections, which are usually penicillin-resistant, treatment can be started with chloramphenicol or erythromycin. However, the rapid emergence of resistant strains of staphylococci to erythromycin, usually within 3 weeks, somewhat limits its use, but when erythromycin is combined with chloramphenicol therapy, resistant strains develop much more slowly. The tetracyclines have very little place in the treatment of severe staphylococcic infections.

In 7 of the 8 patients of this series water-sealed drainage with suction was used. In the very young infant and the small child surgical drainage should be considered immediately when empyema complicates a pulmonary infection. There is no justification for the employment of repeated aspirations as a method of treatment in staphylococcic empyema. Empyema in young infants represents an emergency condition and should be treated accordingly.

Use of Thromboelastography in the Newborn Infant: A Preliminary Study. M. Cordeiro Ferreira and N. Cordeiro Ferreira. Semaine hôp. Paris 35:385-391 (Aug.-Sept.) 1959 (In French) [Paris].

Blood coagulation was studied by thromboelastography in 80 newborn infants, 50 of whom were born at term and 30 were premature infants. Pathological changes in the blood components were recorded in 20 at-term infants. The changes involved deficiency of the prothrombin complex in 10 instances, deficiency of platelets in 5, and deficiency of the antihemophilic factor in 5. None of the infants had the hemorrhagic disease of the newborn. Pathological changes of the blood components on thromboelastographic examination were observed in all the premature infants. Most of the changes entailed the deficiency of the prothrombin complex and the deficiency of platelets in 5 patients.

Thromboelastographic patterns were normal in 2 at-term newborn infants with intracranial hemorrhage. The thromboelastographic pattern showed abnormality in one premature infant with intracranial hemorrhage. Thromboelastographic examination showed normalcy in 2 other newborn infants with hemorrhagic disease. The authors conclude that the etiology of the hemorrhagic disease of the newborn still remains obscure and that neither present improved knowledge about blood coagulation nor the discovery of vitamin K have illuminated the problem.

Experiences with Adrenocorticosteroid Therapy in Allergic Children. H. W. McKay Jr. and S. C. Dees. North Carolina M. J. 20:333-340 (Sept.) 1959 [Winston-Salem].

The authors report on 210 children from a private pediatric allergy practice, who were referred to them for consultation and who were seen as outpatients during the first week of every month in 1958. The records of these children were reviewed for the incidence of allergic and other associated diseases, and they were analyzed with respect to the use of adrenocorticosteroid therapy. Almost every allergic condition known to exist in children had been diagnosed in these patients, that of asthma being made in 155, allergic rhinitis in 183, and atopic dermatitis in 44. Seventy-two (34.3%) of the 210 allergic children were treated at some time during the course of their illness with one or more forms of glucocorticoid therapy. Since topical adrenocorticosteroid preparations are not absorbed in quantities sufficient to produce adrenal suppression or other systemic effects, 20 of the 72 patients who received this type of therapy alone were not further analyzed. The remaining 52 patients were subdivided into 3 groups, namely, 28 patients who received brief systemic adrenocorticosteroid therapy, 16 patients who received systemic adrenocorticosteroid therapy more than briefly, yet for less than 4 months (short-term treatment), and 8 who received systemic adrenocorticosteroid therapy for prolonged periods (long-term treatment). Most of the 52 children who had received systemic treatment with adrenocorticosteroids had this form of therapy before conventional specific treatment was attempted, and in some of them adrenocorticosteroids were used in preference to less powerful, but safer, symptomatic therapy.

Complications observed in 6 of the 8 patients who received long-term adrenocorticosteroid treatment consisted of the changes of Cushing's syndrome, such as moon face, obesity, striae, and increased downy hair over the face, back, and extremities. Six of the 8 patients had arrest of growth; 3 had recurrent abdominal pain, without associated signs of gastroenteritis or other gastrointestinal conditions; 2 had nausea and vomiting: and pseudotumor cerebri or benign intracranial hypertension occurred in two. A threatening infection, with months of recurring furuncles, occurred in one patient in the course of adrenocorticosteroid therapy. Six of the 8 patients were hospitalized 20 times while taking adrenocorticosteroids; hospitalization was necessary for control of allergic symptoms or for complications arising from steroid therapy.

These data show that adrenocorticosteroids are extensively used for treating allergic children before, and as a substitute for, specific allergy treatment. Though prolonged use of adrenocorticosteroids implies more severe allergic disease, the authors feel that the frequency of hospitalizations and the number of complications observed in the long-term treatment group are particularly significant. They are greater than normally would be expected from the severity of the allergic conditions. The serious side-effects and the difficulties of withdrawal after prolonged use so far outweigh the temporary benefits that they detract from the general usefulness of these drugs in allergic children. The continuous use of adrenocorticosteroids for more than short periods of time is hazardous. They should be reserved for acute emergencies and special circumstances.

Study of Two Cases of Phenylpyruvic Idiocy Treated by a Phenylalanine Deficient Diet. J.-P. Christen. Helvet. paediat. acta 14:271-281 (Sept.) 1959 (In French) [Basel, Switzerland].

The author says that at the children's clinic of the University of Lausanne the ferric chloride test is made routinely on the urine of all children admitted with signs of mental deficiency. He presents the histories of 2 sisters, aged 4 years 5 months and 5 years 8 months, respectively, in whom the outcome of the ferric chloride test indicated the presence of phenylpyruvic acid, and led to the diagnosis of phenylpyruvic oligophrenia. The parents of the little girls were first cousins, as is illustrated in a genealogical diagram of the family. The children were below normal in weight and height, and had blue eyes and blond hair. Their skin had the mousy odor characteristic of patients with phenylpyruvic idiocy.

The disorder is due to an enzyme defect of the liver, more particularly to a lack or deficiency of phenylalaninase, resulting in defective oxidation of the oxyphenylalanine or tyrosine. Therefore, the children were put on a diet low in phenylalanine. In the older girl the biochemical disorders, namely, hyperphenylalaninemia, hyperphenylalaninuria, phenylpyruvicaciduria, and hyperaminoaciduria, improved rapidly, but the clinical signs remained unchanged, whereas in the younger girl the biochemical improvement was associated with a noticeable clinical improvement. The author concludes from these observations that a diet low in phenylalanine is effective in the treatment of phenylpyruvic oligophrenia, provided that it can be started early, if possible in the first 2 years of life. If the treatment is postponed, the cerebral lesions become irreversible. The favorable outcome of the treatment depends on an early diagnosis.

Aminophylline Poisoning in Childhood. R. Pollack. J. M. Soc. New Jersey 56:550-552 (Sept.) 1959 [Trenton].

Aminophylline has been used in the treatment of asthmatic conditions, because it exerts a powerful bronchodilating effect. Unfortunately, it is also capable of producing the severest toxic reactions, especially in early childhood. Reports on fatalities from aminophylline have appeared in the literature. The author presents the history of a 9-month-old girl in whom asthmatic bronchitis had been diagnosed. After the intramuscular injection of 300,000 units of penicillin, and of several doses of 125 mg. of tetracycline by mouth, the temperature decreased from 104 to 101 F (40 to 38.3 C), but the respiratory difficulties were still present. The physician prescribed a proprietary suppository containing theophylline (130 mg.), ephedrine hydrochloride (25 mg.), and phenobarbital (12 mg.). This suppository was repeated 5 hours later. A few hours after the second dose of suppository, the baby became extremely restless, and the temperature rose to 106 F (41.1 C). The child was agitated, dyspneic, and cyanotic. A loud expiratory wheeze, dry rales, and rhonchi were heard throughout the chest. A pediatrician diagnosed this as theophylline poisoning. The infant had convulsions off and on until she died.

The findings were similar to those in children with aminophylline poisoning. The suppositories administered to this child contained theophylline rather than aminophylline. However, the author points out that aminophylline is merely theophylline combined with ethylenediamine to enhance its solubility, and theophylline is usually employed as aminophylline. Sensitivity to the drug is not uncommon. The dosage allows only a small margin of safety. Oral administration is reasonably safe, since vomiting is an early development in toxic reaction and eliminates the drug. The ease of ordering rectal suppositories makes this route tempting. Here lies the grave danger of aminophylline poisoning. It is questionable whether the rectal administration of aminophylline is ever indicated.

Severe Functional Disorders of Glomerular Capillaries and Renal Hemodynamics in Treated Diabetes Mellitus During Childhood. G. Stalder and R. Schmid. Ann. paediat. 193:129-138 (Sept.) 1959 (In English) [Basel, Switzerland].

A preliminary report is made on the results of clearance studies in a group of 10 juvenile diabetics. Eight of these patients were between 5 and 15 years of age; one was 18 and another was 26 years old. The duration of the disease varied from one month to 14 years. All the patients were treated with insulin and showed no signs of diabetic nephropathies. The examinations were made in the morning, mostly after the patients had received their regular insulin dosage and breakfast. All the determinations were made at a constant concentration of insulin and para-aminohippuric acid in the plasma. The findings represent the mean values of at least 3 urine collections. It was found that after a diabetic decompensation there existed abnormally changing values of effective renal plasma flow (ERPF), together with inverse changes of filtration fraction (FF) and glomerular filtration rate (GFR). With one exception, the GFR was either in the high normal range or distinctly elevated in all the patients. The shorter the interval after the patient's last prolonged decompensation of diabetes, with or without ketoacidosis, the higher was the GRF. The abnormal clearance values were associated with either renal hyperemia or longstanding renal oligemia.

The GFR, FF, and ERPF values observed in this study were interpreted as an indication of increased glomerular congestion and mechanical distention of the capillary wall, caused by longstanding functional occlusion of the afferent and efferent arterioles. These disorders seem to be reversible. The possibility of a therapeutic approach with reserpine and phthalazine derivatives is now being investigated. It may open a new path to controlling juvenile diabetes and preventing renal-vascular complications.

Clinical Indications for the Prophylactic Treatment of Kernicterus in Prematurely Born Infants (Follow-up Studies on 31 Premature Infants). F. Linneweh and H. Bickel. Klin. Wchnschr. 37:963-966 (Sept. 15) 1959 (In German) [Berlin].

In prematurely born infants hyperbilirubinemia may lead to encephalomyelopathy with icterus (kernicterus). Suspected causes are various toxic and infectious factors. The still inadequate coupling of bilirubin with glucuronic acid, increased permeability of the blood-brain barrier, and the inhibitory effect of bilirubin on the respiration of the brain cells all presumably play a part in the pathogenesis. The hyperbilirubinemia appears on the 3rd or the 4th day of life and reaches a maximum between the 5th and 7th days. A number of investigators have demonstrated that exchange transfusions lower the bilirubin content of the serum, and that kernicterus can thereby be prevented. The bilirubin content of the blood of prematurely born infants has been accepted by most of these workers as indicator of the need for exchange transfusion. Opinions differ, however, about the level of the bilirubin content above which there is danger of the development of bilirubin encephalopathy.

The authors are of the opinion that the increased bilirubin content is only one of several factors responsible for the encephalopathy and that, therefore, the determination of the level of bilirubin in the blood is an inadequate criterion for the advisability of exchange transfusion. They had pointed out several years ago that clinical factors do not always correspond with the "critical" level of the bilirubin content of the blood, and they had found that at the time when the first symptoms of bilirubin encephalopathy appear, the brain lesions have not as yet become irreversible. The early symptoms include refusal to take food, rapid loss of weight, fluctuation in temperature, motor unrest, yawning, and debility.

Follow-up studies are presented on 2 groups of children. One group of 15 patients had been treated by exchange transfusions for hyperbilirubinemia between the 3rd and 7th days of life; the other group of 16 had not received such treatment. Data on both groups, including weight at birth and at the time of follow-up, bilirubin content of the blood, and special symptoms, are tabulated. At the time of follow-up both groups of children ranged in age from 18 to 39 months. The 15 children who had been given exchange transfusions on the basis of clinical symptoms had all developed normally, but the 16 who had not received exchange transfusions had also developed normally.

Kernicterus has been known to develop with blood bilirubin levels of less than 15 mg. per 100 cc. of blood and has failed to develop in infants with levels as high as 30 mg. per 100 cc. The authors deduce from this that 20 mg. per 100 cc. cannot be regarded as the "critical" level for the bilirubin content of the blood, and that the need for exchange transfusion should be decided by the early symptoms of bilirubin encephalopathy. Exchange transfusion involves risks and should be avoided if there are no clinical indications for its use.

ENDOCRINOLOGY

Treatment of Ovarian Dysfunction with Small Doses of Cortisone or Hydrocortisone. W. McK. Jefferies and R. P. Levy. J. Clin. Endocrinol. 19:1069-1080 (Sept.) 1959 [Springfield, Ill.].

Because mild hirsutism or a high level of urinary 17-ketosteroid excretion is often observed in women with functional irregularities of menstruation, the possibility exists that there may be an associated mild disorder of adrenocortical function. If such were the case, treatment with suitable doses of cortisone or hydrocortisone might be beneficial. One of the authors had obtained encouraging results with the oral administration of either of these steroids in doses ranging from 2.5 to 5 mg. given at intervals of 8 hours or less to women with hirsutism and infertility. This led to an extension of the trials to include any patient with irregularity or absence of menstruation on a functional basis. Among 52 such women, between the ages of 17 and 36 years, oral administration of cortisone acetate or hydrocortisone resulted in resumption or increased regularity of ovulation in 46 (89%). Of 38 patients in this series who had associated infertility, 21 (55%) had one or more pregnancies while receiving this type of treatment. No untoward effects were observed. In some patients, hirsutism, acne, or chronic cystic mastitis also improved.

The results suggest that in an appreciable number of patients with ovarian dysfunction this condition may be related to a mild disorder of adrenocortical function, and indicate that continued low-dosage adrenocortical steroid therapy is a practical and effective treatment for such patients. The effective dosage has been found to vary with individual patients; it ranges from 2.5 to 5 mg. 4 times daily, the most frequently effective dose being 5 mg. every 8 hours.

Sex Reversal in Men Revealed by Nuclear Sex Determination in Neutrophil Leukocytes. I. Halbrecht. Harefuah 57:25-27 (July 15) 1959 (In Hebrew with English Summary) [Tel Aviv, Israel].

The author presents a preliminary report on the results of nuclear sex determination in newborn infants, in men with azoospermia, and in women with various sexual disturbances. The method used for nuclear sex determination was that described by Davidson and Smith. With the aid of this method a morphologic difference between the polymorphonuclear neutrophil leukocytes in the male and those in the female was revealed. The difference consists of a solitary chromatin nodule with a drumstick form, which becomes separated from the main nuclear lobes in a proportion of the neutrophils and is found only in those of the female. In 100 normal newborn infants of both sexes, the nuclear sex was found to be identical with the phenotypic sex. One out of 8 newborn infants with hypospadias was found to be chromatin-positive (female). None of the women with various menstrual disorders (primary or secondary amenorrhea), hirsutism, and nanism showed discrepancy between their nuclear and their phenotypic sex. Five of 24 men with azoospermia were found to be chromatin-positive (female nuclear sex).

Familial Male Pseudohermaphroditism with Labial Testes and Partial Feminization: Endocrine Studies and Genetic Aspects. H. A. Lubs, O. Vilar and D. M. Bergenstal. J. Clin. Endocrinol. 19:1110-1120 (Sept.) 1959 [Springfield, Ill.]

The authors report on a family in which there were 5 male pseudohermaphrodites in 2 generations. In the 2 sibling groups that were studied, all males were pseudohermaphrodites; in the other groups, all males were reported as normal by the family. The females were normal. Of the 5 male pseudohermaphrodites, 2 were adults, aged 28 and 26 years, 2 were children, aged 6 years and 13 months, and 1 was a 16-year-old youth. The pattern of abnormalities was remarkably constant, considering the variation in age; each affected male had en enlarged clitoris, labia with varying scrotal characteristics, and a urogenital sinus containing the urethra. In the 2 adults there were histologically proved testes, female breast development, female hair distribution, and labial testes. In the 16-year-old patient, who was not studied by the authors, the sex organs and secondary sex characteristics were identical with those of the 2 adults, as stated by the family physician. In the 2 affected children, the testes had almost descended to the labia in the older child, and were not palpable in the infant. In the 3 patients who were examined by buccal smear, the cellular nuclei were chromatin-negative (male nuclear sex). The testes and epididymis had been removed, in view of a proposed marriage, from one of the adult patients who had been reared as a girl; repeated attempts to stain these organs for alkaline phosphatase yielded negative or faintly positive results. This absence of alkaline phosphatase in the testes on histochemical determination was an unexplained and unexpected finding.

It may well be that there are multiple causes of male pseudohermaphroditism and that it is a mistake to attribute a common causation to the clinical spectrum extending from hypospadias to phenotypic females with testes. Witschi, Nelson, and Segal, in a recent discussion of this problem, concluded that a maternal antitestis factor transmitted in utero to all male fetuses offered the best explanation of the genetic behavior of such families. This factor, resulting from a dominant trait in a heterozygous mother, would also be passed on to half of her daughters. This explanation also affords an adequate explanation for the family reported here. No information about the nature of the antitestis effect was obtained from this family.

Haemophilia A in a "Girl" with Male Sex-Chromatin Pattern. I. M. Nilsson, S. Bergman, J. Reitalu and J. Waldenström. Lancet 2:264-266 (Sept. 5) 1959 [London].

Classical hemophilia (antihemophilic globulin deficiency) is transmitted by a sex-linked recessive gene and is very rare in females. The hemozygous hemophilic state in the female can result from the marriage of a hemophilic man to a woman who is a carrier of the disease. Four such cases of true hemophilia in the female have been reported. Seeming exceptions to strict sex linkage in hemophilia have not been explained, and mutation has been suggested as a possible cause. The authors report a 16-month-old girl with severe hemophilia A. Three possibilities were considered to explain the apparent exception from sex-linked inheritance: 1. The child might be a homozygous hemophilic female by inheritance or mutation. 2. The child might be a heterozygous female (carrier) with unusual bleeding tendency. 3. The child might have a male chromosomal pattern. Heterozygous inheritance of the hemophilic gene was possible, since the mother was a true carrier of hemophilia A; but homozygous inheritance was unlikely, since the father was not affected and nothing suggested that the child was not his offspring.

The child had symptoms of severe hemophilia A with an antihemophilic globulin (AHG) activity of only 0.1%. Her coagulation values were also the same as those found in the hemophilic male relatives in her family. The female carriers in the family, on the other hand, had AHG values of 25 and 35% and no bleeding symptoms. The occurrence of hemophilia in this girl, who might be heterozygous for the hemophilic gene, could be due to a mutation of the other X chromosome, resulting in a homozygous female. This possibility was eliminated by chromosome studies which showed that the patient did not have a XX chromosomal constitution.

The chromosome studies showing a male sex-chromatin pattern offered the explanation. Tissue culture of skin specimens and cytological studies showed 46 chromosomes and a probable XY sex chromosomal constitution. Two possible genetic constitutions must be considered—XY or XO. According to the first alternative, the patient is a chromosomal male. According to the second, the patient could be a female with a chromatin-negative Turner's syndrome, in which the bone marrow cells proved to contain 45 chromosomes and in which the sex chromosomal constitution was determined as XO. But the child had no congenital malformations, such as digital anomalies, webbed neck, or evidence of heart disease, which are common in Turner's syndrome.

The possibility that the child is a hermaphrodite cannot be determined until she has reached sexual maturity. It appears probable that the sex chromosomal constitution of the patient is XY. The authors suggest that similar cases might have been published without complete clarification. The case presented demonstrates that seeming exceptions from sex-linked inheritance may, in reality, conform to the genetic pattern that would be expected. It also confirms the correctness of leukocyte sex determinations and chromosome maps, since the single X chromosome found was marked by a sex-linked genetic trait.

OPHTHALMOLOGY

Visual Disturbances in Pernicious Anemia. E. M. Verveen-Keulemans. Nederl. tijdschr. geneesk. 103:1749-1752 (Aug. 29) 1959 (In Dutch) [Amsterdam].

On the basis of the history of 2 men, both 62 years old, the author directs attention to the fact that impairment of vision sometimes is an early symptom of vitamin B_{12} deficiency and that it may precede the other symptoms of pernicious anemia. The first of the 2 patients had been under the care of an ophthalmologist because of reduced visual acuity, and a neurologist had suggested that his complaints might be of vascular origin, or due to a vitamin B_{12} deficiency. Injections of vitamin-B complex effected some improvement, but the dose was inadequate for complete cure.

The second patient, who complained of diarrhea, emaciation, and lack of appetite, was examined by an internist and a neurologist, both of whom were unable to establish a diagnosis. Later he was referred for internistic examination by an ophthalmologist, whom he had consulted on account of impaired vision. He now complained of headaches, insomnia, loss of memory, and tingling sensations in arms and legs. He was a heavy smoker. Examination revealed impairment of the reflexes and reduced visual acuity. The erythrocyte count was 2.6 million per cubic millimeter, the color index was high, and anisocytosis and poikilocytosis were found. Furthermore, tests of the stomach revealed achlorhydria. On the basis of these findings pernicious anemia was diagnosed, and treatment was instituted. A reticulocytic crisis followed, and there was subjective and neurological improvement, but there was no change in the impaired vision. It is assumed that the vitamin B_{12} deficiency caused optic atrophy, which apparently was no longer reversible. Heavy smoking may have aggravated the symptoms.

Reports in the literature indicate that visual disturbances may arise in all forms of vitamin B_{12} deficiency and that they are intensified by smoking. Prognosis depends on the time the diagnosis was made and treatment instituted.

Heterograft of Fish Cornea into Rabbit Eyes. J. Tsutsui and S. Watanabe. Am. J. Ophth. 48:363-368 (Sept., part 1) 1959 [Chicago].

Keratoplasty with heterografts was attempted more than 100 years ago. The authors used fish corneas for interlamellar transplantation into rabbit corneas. The grafts, 8 mm. in diameter and 0.3 to 0.8 mm. thick, were taken from perch, mackerel, gray mullet, bonito, and Seriola fishes. Some of the grafts were pretreated with a rabbit serum in a refrigerator for 24 hours. After a slight donor-recipient reaction, transparent heterografts were obtained in 10 rabbits out of 12. The other 2 grafts of fish cornea became opaque almost immediately after the operation. In control experiments, 2 human, 1 dog, and 2 ox corneas were grafted into rabbit corneas. All these mammalian grafts became opaque in from 3 to 10 days. Because of the high rate of success with fish corneas and the complete failure with mammalian corneas, the authors believe there is evidence that, the farther apart phylogenetically the donor and the recipient are, the less likelihood there is that a donor-recipient reaction develops. The postoperative donor-recipient reaction seemed to be more intensive when a fresh graft was used. Fish cornea stored for a few days in ice seemed suitable; if the cornea was stored for more than 10 days, the results were unfavorable. This suggests that an adequate denaturation of the proteins may decrease the antigenicity. A preoperative serum treatment of the graft appeared to have no influence on the fish cornea. In the successful fish cornea grafts, the process of organization of the grafted tissue into the recipient cornea appeared one month after the operation and was completed 5 or 6 months later.

Embolism of the Central Retinal Artery: Originating From an Endocardial Myxoma. W. A. Manschot. Am. J. Ophth. 48:381-385 (Sept., part 1) 1959 [Chicago].

A 57-year-old man suddenly became subcomatose during the night. The following morning, on admission to the hospital, he showed spastic paresis of the right half of the body with right-sided central facial paresis. The left eye showed a choked disk and a recent "focus of inflammation" between the disk and the macula; the picture was highly suggestive of juxtapapillary chorioretinitis. The patient died 3 days later. An autopsy showed extensive encephalomalacia of the left cerebral hemisphere. The left internal carotid artery was filled, from a point 1.5 cm. before the entry into the circle of Willis, by an embolus which continued into the left middle cerebral artery. The trunk and the large rami of the central retinal artery and some posterior ciliary arteries were also occluded by emboli. These emboli originated from an endocardial myxoma localized in the left atrium.

OTOLARYNGOLOGY

Otogenic Meningitis in Infancy and Childhood in the Antibiotic Era: Observation on 38 Children Treated at Los Angeles County General Hospital from 1950 to 1957. H. J. Hara. A. M. A. Arch. Otolaryng. 70:315-320 (Sept.) 1959 [Chicago].

The authors report on 24 boys and 14 girls with otogenic meningitis, who were treated on the otolaryngologic service of the Los Angeles County General Hospital between 1950 and 1957. Of the 38 children, 19 were aged less than one year, 4 were between the ages of 1 and 2 years, 7 were between the ages of 2 and 5 years, 5 were between the ages of 5 and 10 years, and 3 were between the ages of 10 and 13 years. Nineteen children recovered, and 19 died. Of the 19 patients who died, Diplococcus pneumoniae was isolated as the causative organism in 8, Hemophilus influenzae in 4, and Neisseria meningitidis (meningococcus) in 2; the causative agent was unknown in 5. When hospital treatment was instituted within 24 hours after the onset of meningitis, the recovery rate was 67%. When this was delayed 2 to 4 days, the recovery rate was 56%. In those patients who did not receive treatment until 5 days or longer, the rate was reduced to 36%.

Meningitis was secondary to acute otitis media or concurrent with acute otoantritis. Masking of symptoms of acute otitis media was the chief cause of delay in diagnosis. This, in turn, contributed to a high mortality rate in this series. The key to the solution of reduction of morbidity and mortality of otitic meningitis has been earlier recognition of the meningeal symptoms and prompt institution of adequate and appropriate chemotherapy. Broad-spectrum antibiotics became available in 1953 and have been freely used in conjunction with the sulfonamides and penicillin. Intrathecal administration was not practiced.

Tracheal Fenestration Operation For Pulmonary Insufficiency: Preliminary Observations. F. A. Hughes Jr., W. F. Jones, R. E. Campbell and others. J. Tennessee M. A. 52:356-359 (Sept.) 1959 [Nashville].

The authors define Rockey's tracheal fenestration as a surgically created, epithelized opening into the cervical trachea, which is partially or completely closed by skin folds or valves. They list the advantages of this fenestration over conventional tracheostomy and explain the mode of action of tracheal fenestration in pulmonary insufficiency. The clinical course of a patient with low pulmonary reserve is characterized by recurrent attacks of what is best described as a "hypoventilation crisis." This may end in sudden apnea and asphyxia or lead to slowly progressive cor pulmonale and cardiopulmonary failure. Patients surviving these attacks may be restored to a status quo and continue to live within the limits of their low pulmonary reserve until the next crisis arises. Mostly, however, each attack further diminishes cardiopulmonary reserve Hypoventilation crises are usually precipitated by respiratory infection, by oversedation, by excessive oxygen inhalation, or by mild congestive failure. Such circumstances usually bring on an increase in bronchial secretion. Failure to eliminate this promptly leads to stagnation, inspissation, and increased viscosity of secretions, resulting in progressive bronchiolar obstruction, increased trapping of air, and decreased respiratory function. Tracheal fenestration, making possible efficient intubation and aspiration, can break the vicious cycle and terminate the hypoventilation crisis.

The authors performed 4 fenestrations and 2 permanent tracheostomies in the past 9 months. Several other patients were so acutely ill that emergency tracheostomy only was performed, but tracheal fenestration will be performed later in some of these patients. In the first 3 fenestrations performed by the authors, the stomal skin flaps differed from Rockey's, and a tracheostomy cannula was placed through the window. In these cases only one skin flap survived; nevertheless, the occlusion of the stoma allowed normal phonation. The most recent fenestration was performed by Rockey's technique with the use of 4 flaps. No tracheostomy cannula was inserted, and the flaps healed well. Further experience with the procedure is needed to define better the most desirable operative technique, the indications and contraindications, and the prognosis.

Temporal and Pitch Aspects of Superior Esophageal Speech. J. C. Snidecor and E. T. Curry. Ann. Otol. Rhin. & Laryng. 68:623-636 (Sept.) 1959 [St. Louis].

Utilizing a sensitive electropneumograph and phonophotographic techniques, the authors studied the time and pitch factors in 6 esophageal speakers with superior speaking performance. Speakers with superior performance were selected, so that any generalizations arrived at might serve as suitable goals for those learning to speak without a larynx. All the speakers were men with at least 4 years' experience with esophageal speech. They spoke with continuity and without consciousness of the act of swallowing and eructation. They spoke easily, and their speech was produced without apparent thought or effort, similar to that of normal speakers. Three speakers counted to 4, 7, and 8, respectively, and 3 speakers counted to 10 on one air-charge, in the 3 trials allowed each speaker. The speakers averaged 5 words per air-charge, and performances averaged about 120 words per minute. A top limit of 11 or 12 syllables is very satisfactory. However, one speaker achieved an extreme range of 22 syllables.

The air-charge was gulped in about one-half second, a more rapid performance than that of the normal speaker inhaling for an intraphrasal breath pause. There was a difference of almost exactly one full octave between the frequency levels of the esophageal speakers with superior performance and those of the normal adult male speakers with superior performance, the respective median values being 63.27 and 132.1 cps. Pitch inflections, shifts, and total and functional pitch range were within the normal limits for normal male speakers. The rate of pitch change, in tones per second, was only half that of the normal speaker.

The results obtained established realistic norms for those who must learn to use esophageal speech. Highly efficient air-charges encompassing many syllables, as reported in recent popular literature, were not apparent. Contrary to some reports, pitch variability was comparable to that in normal speech. It is, however, very doubtful that the average pitch level can be raised much, if any, above 66 to 77 cps.

Speech Defects Following Adenotonsillectomy. W. J. Roberts. Rocky Mountain M. J. 56:67-69 (Sept.) 1959 [Denver].

Closure of the velopharyngeal orifice on swallowing or in valving of the emitting air column so as to form such consonants as "g," "c," or "k" is affected by a combination of muscle actions. The author explains these and points out that occasionally after adenotonsillectomy, but also after cleft palate surgery, uvulectomy, or surgery for repair of traumatic wounds of the soft palate, the lateral and the posterior pharyngeal walls, a patient will have an inadequate velopharyngeal closure and thus exhibit hypernasal speech, similar to that observed in children with cleft palate. Temporary hypernasal speech defect may result merely from a reflex inhibition of the muscles of the palate and pharynx from pain. This phenomenon subsides rapidly as sore throat subsides.

Occasionally the child with reflex inhibition of the velopharyngeal sphincter from pain learns to cultivate a "protected" speech because of emotional and psychological reasons and a desire for attention. Actual hysteria may be present. The child recovers his ability to speak normally if his emotional problem is properly met. Inadequate velopharyngeal closure may result also from palatine neuritis with muscle weakness or paralysis due to poliomyelitis, to a neurotropic influenzal virus, and to toxins from Klebs-Loeffer bacillus. Frequently the muscle weakness or paralysis may follow immediately after adenotonsillectomy and take many weeks in recovery. Permanent paralysis may also occur.

In order to avoid the unpleasantness of coping with a hypernasal speech defect after adenotonsillectomy, the surgeon can often be forewarned. He should look out for the child who talks with a high-pitched, squeaky, pinched voice. Parents should be cautioned that a temporary speech defect may result from adenotonsillectomy done on the child with prolonged and severe nasal obstruction, especially if other stigmata of arrested development of the nose, hard palate, and upper alveolar arch are present. Observing the motion of the palate and palpating the hard palate for bony defects before surgery may save much embarrassment postoperatively. Adenotonsillectomy should be avoided if poliomyelitis is present or if influenzal viral infections with a strong neurotropic tendency are prevalent. Adenoidectomy should not be started until anesthesia is deep enough to abolish the swallowing reflex and all muscular motion of the palatal and pharyngeal muscles has ceased. The more complete and thorough the adenoidectomy, the greater the chance for a temporary speech defect.

Traumatic Stricture of the Larynx. L. R. Cranmer. Ann. Otol. Rhin. & Laryng. 68:613-622 (Sept.) 1959 [St. Louis].

The authors report on 3 male patients, between the ages of 14 and 56 years, and a 35-year-old woman who sustained laryngeal injuries in automobile accidents, and on a 64-year-old man with laryngeal obstruction caused by inadvertent removal and traumatic reinsertion of an intratracheal tube in the course of abdominal surgery. Of the 4 patients who had automobile accidents, the first sustained a blow to the neck, with marked cervical swelling, tenderness, and progressive dyspnea, requiring tracheotomy 4 hours after the injury. Complete respiratory obstruction resulted when the initial incision was made, which opened an anomalous jugular venous arch. A large amount of blood was aspirated from the trachea and bronchi. Slow decannulization was complete after 3 weeks, and persistent fixation of the left vocal cord was noted. In the second patient, contusion of the neck was accompanied by a transverse laceration of the base of the epiglottis, so that it overhung the larynx, producing obstruction. There was also unilateral cricoarytenoid dislocation and fixation. Permanent hoarseness resulted. The third patient struck the front of his neck against the dashboard. Tenderness, swelling, and immediate hoarseness were first treated by bed rest, but progressive laryngeal obstruction during the next week made an emergency low tracheotomy necessary. There was great mucosal swelling nearly obliterating the lumen. After several days a core mold was introduced, and triangular laryngeal dilators were used at the time of changing core molds to larger sizes over a period of 6 months before extubation could be accomplished successfully. The fourth patient struck her neck, and cervical subcutaneous emphysema, ecchymosis, and mild inspiratory stridor were followed by increased dyspnea. Tracheotomy and internal splinting with a plastic core mold were done. At the time of tracheotomy a laryngofissure was performed. There was tremendous thickening of the criothyroid membrane. A vertical and intersecting oblique fracture line was found. An unsuccessful attempt to reduce an anterior cricoarytenoid dislocation was made. Direct interosseous fixation of the thyroid fragments was done. The internal splint treatment was complicated by one of the core molds slipping entirely through the larynx and coming to rest on top of the tracheotomy tube. Endoscopic removal was unsuccessful, and the neck had to be reopened to retrieve the dilator. Follow-up examination revealed severe hoarseness from anterior webbing and the persistently tipped and fixed arytenoid cartilages.

Laryngeal injuries are assuming greater importance because of automobile accidents and their high morbidity and mortality. That they are not commoner is mainly because of the protected position of the larynx. There are various types of open and closed injuries varying widely in severity. Early treatment is directed at maintaining the airway with tracheotomy, prevention of stenosis, internal splinting, and careful repair of lacerations. Later cicatricial stenosis may indicate reconstructive surgery. Rehabilitation is not complete without speech therapy for persistent hoarseness.

THERAPEUTICS

A Critical Appraisal of Oral Hypoglycemic Agents. T. H. McGavack. J. Am. Geriatrics Soc. 7:681-697 (Sept.) 1959 [Baltimore].

The author studied 5 orally administered hypoglycemic agents—carbutamide, chlorpropamide, tolbutamide, metahexamide, and phenformin hydrochloride (DBI). Carbutamide has already been discarded as too toxic for human use. Tolbutamide has been extensively employed in as many as 300,000 diabetics according to its manufacturer. Chlorpropamide has recently been released for general use. Metahexamide has been administered to several hundred patients in Europe and to about 300 in this country; prospects for its widespread application seem promising. Of the guanidine derivatives, synthalin was tried in the late 1920's but was considered too toxic for human use because of the incidence of hepatitis. Today its congener DBI is also poorly tolerated by the gastrointestinal tract, although no serious involvement of the liver has as yet been recorded in a limited number of cases. None of these oral hypoglycemic agents is a substitute for insulin. All of them act upon both the pancreas and the liver, but the nature of the activity is still obscure. They are useful in a small percentage of diabetics, of the so-called stable type, who require both insulin and a well-controlled diet to maintain optimal health. The long-term effects on the capacity of the pancreas to produce insulin and on the enzyme systems of the liver concerned with carbohydrate metabolism are not yet known.

Hydroflumethiazide: A New Oral Diuretic. C. J. Edmonds and G. M. Wilson. Lancet 2:303-308 (Sept. 12) 1959 [London].

The action of hydroflumethiazide, chlorothiazide, and hydrochlorothiazide was studied in 2 normal men. It was found that hydroflumethiazide was at least 10 times as effective, weight for weight, as chlorothiazide; it caused more prolonged diuresis of water and sodium, and produced less bicarbonate but more chloride excretion. Its action closely resembled that of hydrochlorothiazide. Hydroflumethiazide was also an effective diuretic in the majority of 30 patients with various conditions, such as pulmonary heart disease (in 7), ischemic heart disease (10), cardiac failure associated with thyrotoxicosis (3), chronic rheumatic heart disease (7), nephrosis (1), and hepatic cirrhosis with ascites (1). There was no diuretic response in the patient with nephrosis, and the results obtained in the patient with hepatic cirrhosis with ascites were also disappointing. Failure to respond to hydroflumethiazide was usually associated with impaired renal function, as shown by an increased blood urea level. Hydroflumethiazide was remarkably free of disturbing side-effects other than a tendency to produce hypopotassemia. There were no signs of digestive disturbances, no changes in the hemoglobin values or in the number of leukocytes, and no albuminuria or other urinary abnormality.

It is essential that the serum potassium level should be watched in patients on continuous oral diuretic therapy. In cirrhosis with fluid retention especial care has to be taken, as a considerable fall in serum potassium may occur within a few days. In the patients of this series a low serum potassium level was not associated with any obvious harm, but it is a hazard, particularly if other drugs (such as digitalis) are being used.

The Clinical Use of Chlorambucil: A Critical Study. D. G. Miller, H. D. Diamond and L. F. Craver. New England J. Med. 261:525-535 (Sept. 10) 1959 [Boston].

The authors report on 38 patients with Hodgkin's disease, 19 with chronic lymphocytic leukemia, and 6 each with lymphosarcoma, reticulum-cell sarcoma, and chronic granulocytic (myelocytic) leukemia, who were treated with chlorambucil, a nitrogen mustard derivative, at the Memorial Center for Cancer and Allied Diseases in New York. The usual starting dose of the drug, administered orally to these patients, was 0.2 mg. per kilogram of body weight, except for the patients with chronic lymphocytic leukemia and those in whom bone-marrow function was compromised because of myelophthisis or previous therapy, who were given 0.1 mg. per kilogram of body weight. The hemoglobin value, white blood cell count, and platelet level were checked after one week and again at 3 weeks. At that time the patient was evaluated for adjustment of the dose. The entire daily dose of chlorambucil was usually taken in the morning, one hour before breakfast, with water only.

Of the 38 patients with Hodgkin's disease, 32 had objective evidence of the disease; of these, 11 (34.4%) had a marked response to their first course of chlorambucil therapy, 8 (25%) had a moderate response, and 13 (40.6%) had no significant response. Nine patients with Hodgkin's disease received second courses of chlorambucil therapy, and 6 had a significant response. Objective improvement resulted from chlorambucil therapy in all 6 patients with lymphosarcoma. Of the 6 patients with reticulum-cell sarcoma, 2 showed a marked response, while the others showed slight or no response. Of the 6 patients with chronic granulocytic leukemia, 5 showed marked response and 1 showed moderate response. Of the 19 patients with chronic lymphocytic leukemia, 6 showed marked response, 6 showed moderate response, and 7 showed slight or no response. The total mean dose of chlorambucil required to achieve maximum results was 5.3 mg. per kilogram of body weight in the patients with reticulum-cell sarcoma, 8.7 mg. in those with chronic lymphocytic leukemia, 10.9 mg. in those with lymphosarcoma, 13.2 mg. in those with Hodgkin's disease, and 26.7 mg. in those with chronic granulocytic leukemia. The mean time necessary to achieve maximum results in the patients studied was 35 days in patients with reticulum-cell sarcoma, 78 days in those with chronic lymphocytic leukemia, 84 days in those with lymphosarcoma, 77 days in those with Hodgkin's disease, and 109 days in those with chronic granulocytic leukemia.

The results obtained show that, with proper adjustment of dosage, chlorambucil is as effective as other alkylating agents in the treatment of Hodgkin's disease, lymphosarcoma, reticulum-cell sarcoma, chronic lymphocytic leukemia, and also chronic granulocytic leukemia. As an alkylating agent for oral administration, chlorambucil has an advantage over triethylene melamine in that absorption is more consistent and not related to food intake, and the effect on the bone marrow is more easily controlled. Chlorambucil may be given safely to patients with chronic leukemia and lymphomas to the point of early bone-marrow depression in an effort to achieve maximum results. With proper adjustment of dosage, maintenance therapy is feasible and, in certain cases, desirable. Untoward side-effects are few, but close observation of the hemoglobin value, white blood cell count, and platelet level is mandatory.

Diphtheria and Tetanus Toxoids Combined with Pertussis and Poliomyelitis Vaccines: Clinical Trial of a Quadruple Antigen. R. J. Wilson, G. W. O. Moss, F. C. Potter and D. R. E. MacLeod. Canad. M. A. J. 81:450-453 (Sept. 15) 1959 [Toronto].

Fifty-one infants received 4 injections of diphtheria and tetanus toxoids combined with pertussis and poliomyelitis vaccines in what is referred to as DPT polio vaccine. Twelve children were 3 months of age; 21, 4 months; 6, 5 months; and the remaining 12 ranged in age from 6 to 12 months. Eight control children received poliomyelitis vaccine alone from the master lot used in the preparation of the DPT polio vaccine. Each infant received 3 doses of DPT polio vaccine, or poliomyelitis vaccine alone, at intervals of 4 weeks. Infants under 6 months of age received a first dose of 0.5 ml. and 2 additional doses of 1.0 ml. Infants over 6 months of age received 3 doses of 1.0 ml. No undue reactions were observed. The fourth dose of 1.0 ml. was given to all 51 infants 12 months after the initial 3 doses.

Before vaccination, approximately 50% of the infants possessed poliomyelitis antibodies, presumably of maternal origin. Vaccination was followed by a marked shift in antibody levels for the 3 types of poliomyelitis virus. The median titer rose from 4 to 64 in type 1 and from 4 to 128 in types 2 and 3. After vaccination, 85% of the infants responded to type 1 poliomyelitis vaccine component and more than 90% to types 2 and 3. All the children responded well to diphtheria and tetanus toxoids. While the presence of maternal immunity interfered in some measure with the response to poliomyelitis vaccine and to diphtheria toxoid, the fourth dose caused the recall type of response and established a sound immunity. The authors believe that the fourth dose, or first recall dose, should be considered essential in establishing immunity in infants and that the first dose of DPT polio vaccine should not be reduced in infants under 6 months of age, in order not to diminish the volume of type 1 poliomyelitis vaccine component.

Prochlorperazine in Airsickness. G. S. Backenstoe. Pennsylvania M. J. 62:1341-1343 (Sept.) 1959 [Harrisburgh].

In a cooperative study carried out by 71 members of the Flying Physicians Association and the Civil Aviation Medical Association, 396 patients known to be susceptible to airsickness were given prochlorperazine before and/or during flight. Of these patients, 261 had previously been treated, often unsatisfactorily, with agents other than prochlorperazine. Good or excellent responses were seen in 307 (77%) of the 396 patients; in 165 (63%) of the 261 patients previously treated with other agents, prochlorperazine produced more satisfactory results. Side-effects, chiefly mild and transient drowsiness, were seen in 32 (8%) of the patients. There were no serious side-effects. The preferred dosage was one 5-mg. tablet given one hour before flight, although many patients were given 10 mg. before flight or 5 mg. 3 times a day. In general, there was no apparent advantage to increasing the dosage beyond this. Prochlorperazine appears to be a highly effective antiemetic, antinauseant, and psychotherapeutic agent. This combination of effects makes the drug especially useful for the treatment of airsickness, where psychic factors often play a major causative role.

The Use of Prochlorperazine in Seasickness. W. L. Wheeler Jr., J. M. Howland, W. Smith and J. E. Corso. Indust. Med. 28:405-406 (Sept.) 1959 [Chicago].

Because most effective antimotion sickness drugs are either phenothiazine or piperazine derivatives, the authors thought that prochlorperazine compound, containing both phenothiazine and piperazine structures, might counteract motion sickness. They evaluated this drug in seasickness among passengers on Grace Line vessels. Each of the 3 vessels used in this evaluation is equipped with hospital facilities and staffed with a ship's surgeon. Because each of the vessels accommodates a maximum of only 52 passengers, the ship's surgeon is immediately available to any passenger who may require treatment, and he can observe the progress of any patient.

During a 10-month period 122 passengers (30 male, 92 female), in whom symptoms of motion sickness developed, were treated with prochlorperazine. Forty-seven patients had vomited at least once before reporting to the ship's hospital; the remaining 75 were experiencing nausea and one or more of the other symptoms of motion sickness, such as dizziness, sweating, pallor, salivation, or changes in blood pressure and heart rate. After questioning and physical examination to exclude disorders other than seasickness, patients were given prochlorperazine orally in 10-or-15-mg. sustained release capsules, or intramuscularly in doses of from 5 to 10 mg. The parenteral form was used in the more severe cases of vomiting, and was discontinued as soon as the patient was able to retain oral medication. Ninety-seven patients received oral doses only. Initially, each patient was given one dose of prochlorperazine (either orally or intramuscularly) and was supplied with 1 or 2 capsules with instructions to take one capsule every 12 hours thereafter, as needed. Ten patients were given placebo capsules initially; 6 of these patients eventually received prochlorperazine orally.

One hundred two patients (83.6%) experienced good results; 19 (15.5%), fair results; and 1 (0.9%), poor results. There were no significant differences in the results reported by each of the investigators. In general, the first dose of prochlorperazine completely controlled all but the more severe symptoms of nausea and vomiting within one-half hour after intramuscular administration, and within 1 or 2 hours after oral administration. Patients with severe vomiting generally obtained results after the second intramuscular dose, given 3 or 4 hours after the first. As nausea and vomiting subsided, patients became active and were able to take food and fluids orally.

Dexamethasone. F. D. Hart, J. R. Golding and G. Brown. Lancet 2:255-257 (Sept. 5) 1959 [London].

The cortisone molecule has been repeatedly modified with the aim of varying its clinical actions and diminishing its so-called side-effects. This report is concerned with dexamethasone, in which a new radical, namely, a methyl group, is introduced at the C16 position. The authors compared dexamethasone with prednisolone in its effect on 30 patients with rheumatoid arthritis in a dose ratio of 1/5 over periods of up to 24 weeks. Little difference was apparent, 12 patients preferring dexamethasone, 12 preferring prednisolone, and 6 being indifferent. Dyspeptic symptoms appeared to be no less common with dexamethasone than with prednisolone. Little or no difference was noted in therapeutic response to the 2 drugs in 3 patients with lupus erythematosus, in 2 with scleroderma, in 1 with ulcerative colitis, and in 1 with status asthmaticus. One man, who had had ankylosing spondylitis for 16 years, had been treated with prednisolone for 16 months. On transferring to dexamethasone, he became symptom-free, but on returning to prednisolone, he suffered a relapse. Thus, while in most cases there was no obvious advantage in transferring to dexamethasone, some patients nevertheless preferred it. Their conditions improved on the administration of dexamethasone, and it is, therefore, useful to have yet another potent steroid available.

Progress with New Antileprosy Drugs. T. F. Davey. Internat. J. Leprosy 26:299-304 (Oct.-Dec.) 1958 [New Orleans].

There is no place in drug trials in leprosy for the control patient who is simply given a placebo. Any new drug must be judged against the standard set by diaminodiphenylsulfone (DDS) and will be of interest only if it has some advantage over DDS, either through increased activity or in freedom from toxic action. It was formerly the practice to choose as controls in drug trials patients corresponding in type and intensity of their infection to those volunteering to participate in a trial, and give them standard DDS treatment. A more satisfactory method, and one that appears to meet all circumstances, consists in bringing together the records of as large a number of patients as possible who have had continuous DDS treatment, and producing graphs showing the average decline in bacterial index during DDS therapy at the center concerned. Provided the numbers contributing to it are adequate, such a procedure provides a simple but reliable standard against which it is possible to check the progress of any individual patient, or any group, and thus it becomes possible to compare progress under one new drug with that under another.

Over several years a standard of this nature has gradually been built up by the author at Uzuakoli in eastern Nigeria. He illustrates the procedure in studies on 3 new antileprosy drugs. The first, the thiourea compound Ciba 1906 (DPT), was studied for 3½ years. It proved to be an active and valuable drug, and during the first 6 months it was decidedly superior to DDS; thereafter its activity approximated that of DDS. The second drug, diaminodiphenylsulfoxide (DDSO), proved slower but very steady in action and had advantages and disadvantages compared with DDS. The third drug, diethyldithiolisophthalate (ETIP), also known as compound 15,688, has a remarkable effect in some patients, producing a phenomenal change in the bacterial index and in the morphology of bacilli for a very short time, after which drug resistance develops. By the judicious use of these drugs during their period of optimal activity, associated where appropriate with DDS, it may be possible to attain new levels of effectiveness in the chemotherapy of leprosy.

Erythromycin Prophylaxis: A Four Year Study. R. A. Tidwell and D. Lewis. Antibiotic Med. 6:395-400 (July) 1959 [New York].

The authors administered erythromycin orally as a prophylactic agent over a period of 4 years to 100 children, between the ages of 3 months and 15 years; these children, who were from the outpatient department of the Children's Orthopedic Hospital in Seattle, were being treated primarily for such recurrent illnesses as cystic fibrosis, congenital heart disease, asthma, and recurrent respiratory infections. Each child received either a teaspoon of erythromycin sirup (125 mg.) or one tablet (100 mg.) once daily. Throat cultures were taken during the prophylactic trial, to ascertain the frequency of the appearance of group A beta-hemolytic streptococci and coagulase-positive staphylococci. Cultures were also obtained at frequent intervals from members of the family accompanying these children to ascertain whether or not any unusual Staphylococcus organisms were being implanted in the family group. At no time during the trial were the authors harassed by the appearance of an unusual amount of staphylococci. No relationship could be found between the length of time during which the patient participated in the trial and the appearance of staphylococci in his throat culture, nor could there be found any evidence of increase in daily dosage causing any increase in the incidence of staphylococci. Although the amount of group A beta-hemolytic streptococci was small, nevertheless, comparison with the original cultures would appear to show that, over the period of time involved, there was a very definite decrease in the frequency of the appearance of these organisms.

These findings suggest that erythromycin can be used as a substitute for penicillin in the prophylaxis of group A beta-hemolytic streptococcic disease. The prolonged and continued use of erythromycin does not seem to produce any deleterious effects on the patient, nor does it produce the appearance of coagulase-positive staphylococci that are resistant to erythromycin. There was no demonstrable effect on the staphylococcic pattern of the family group as a result of this prophylactic trial.

PATHOLOGY

Regression Studies with Safflower Oil and Sitosterol in Rabbit Atherosclerosis. J. P. Miller, G. F. Lambert and D. V. Frost. Circulation Res. 7:779-786 (Sept.) 1959 [New York].

The authors induced hypercholesteremia with atherosclerosis in male rabbits by feeding hydrogenated coconut oil as the only lipid in a purified diet. By substituting safflower oil for the hydrogenated coconut oil, they produced a rapid and profound fall in the pasma cholesterol level of the animals. Supplementing the safflower oil with beta-sitosterol at 3% of the oil weight caused an even greater decrease in the plasma cholesterol level. Although in both cases the further development of aortic atheroma was arrested, there was no detectable regression of existing lesions over 24 weeks. Hydrogenated coconut oil feeding alone at first produced unusually high concentrations of liver lipids, including cholesterol, in the rabbits. Very large livers with decreasing liver cholesterol and lipid concentration developed in rabbits surviving on such a diet. This compensation appears necessary for survival. Substituting safflower oil or sitosterol-supplemented safflower oil for hydrogenated coconut oil increased growth rate and decreased concentration and amount of liver lipids, including cholesterol. Addition of a small amount of safflower oil to a hydrogenated coconut oil diet protected in part against elevation of plasma and liver cholesterol levels, even though total fat content of the diet was increased.

Whether these data are indicative of processes occurring in man is a moot question. Everyone is aware that there are species differences with respect to a great many facets of metabolism. Regression studies of atheroma in man are obviously very difficult, if not impossible, to do, and one is anxiously awaiting definitive evidence as to the long-range effects of unsaturated fat administration. While this information is accumulating, animal studies may offer some insight into the general problem and provide clues for further studies in man.

Evaluation of the Adequacy of Needle-Biopsy Specimens of the Kidney: An Autopsy Study. W. F. Kellow, N. J. Cotsonas Jr., B. Chomet and H. J. Zimmerman. A. M. A. Arch. Int. Med. **104**:353-359 (Sept.) 1959 [Chicago].

The authors obtained needle biopsy specimens of the kidney during autopsies performed at the Veterans Administration West Side Hospital in Chicago on 103 deceased patients whose clinical records suggested the presence of renal disease. The representative nature of the biopsy specimens was evaluated by comparison of the histological features and diagnostic conclusions from multiple biopsies with the final autopsy diagnosis. Of 308 biopsy specimens, 235 (76%) accurately reflected the primary histological abnormality, and in 212 biopsy specimens (69%) the correct diagnosis was made. Comparison of the results of needle biopsies on patients with diffuse renal diseases with those on patients with focal diseases showed that an average of 84% of the biopsy specimens obtained from patients with diffuse disease were positive as compared with 51% of those from patients with focal disease. In general, needle biopsy of the kidney is more likely to provide information concerning a specific diagnosis when a diffuse renal disease exists than when the disease is focal.

Antibiotic Susceptibility and Phage Types of Pathogenic Staphylococci: A Study of Two Hundred Ten Strains Isolated at Boston City Hospital in 1955. M. Finland, W. F. Jones Jr. and I. L. Bennett Jr. A. M. A. Arch. Int. Med. **104**:365-377 (Sept.) 1959 [Chicago].

The authors tested 210 strains of coagulase-positive Staphylococcus pyogenes var. aureus, isolated from infected sources in patients at the Boston City Hospital during the latter part of 1955, for their susceptibility to 18 antibiotics. Of the 210 strains, 180 were also subjected to bacteriophage typing. These strains were very uniform in their susceptibility to 10 antibiotics which had never, or only rarely, been used for therapy at this hospital before these strains were isolated, namely, novobiocin, Bryamycin, Streptogramin ("900"), MK 111, neomycin, vancomycin, kanamycin, ristocetin, paromomycin, and bacitracin. In contrast, many of the staphylococci were resistant to 4 of the other 8 antibiotics which had been used extensively in this hospital, namely, penicillin, streptomycin, tetracycline, and erythromycin, and to 3 related drugs, oleandomycin and spiramycin (which are related to erythromycin) and synnematin B (closely related to penicillin). Chloramphenicol was the only widely used antibiotic to which few of the strains were resistant. A considerable greater proportion of the strains resistant to penicillin, streptomycin, tetracycline, and erythromycin were isolated from patients during or after treatment with antibiotics.

Of the 180 staphylococcic strains subjected to bacteriophage typing, 61 (about 33%) were of phage pattern 52/42B/81; slightly more than 25% of the strains were nontypable with the phages used; and the remaining strains were lysed by phages of a large number of single types or patterns. Staphylococci of type 52/42B/81 differed from all others in their susceptibility to penicillin, streptomycin, tetracycline, and erythromycin; nearly all of them were resistant to the first 3 antibiotics, but sensitive to erythromycin. A considerable proportion of the nontypable strains and of those lysed by other phages were resistant to penicillin, streptomycin, and tetracycline, and a smaller number were resistant to erythromycin. Observations on multiple strains of staphylococci isolated from patients during the course of infection, and on changes in their susceptibility to antibiotics, showed that most of the marked differences were related to the introduction or recognition of new strains of different phage types and probably represented mixed infections or superinfections; these new strains were usually, but not always, highly resistant to all the antibiotics that were being used in the patients from whom they were isolated. Occasional decreases in susceptibility to antibiotics were noted in successive isolations of staphylococci of the same phage pattern; in general, these were clearly related to the antibiotics in use.

These observations support the concept that the increasing incidence of staphylococci resistant to various antibiotics is a consequence of the widespread use of antibiotics. From the practical point of view it is important to obtain repeated cultures from patients with staphylococcic infections during antibiotic therapy and to study the strains from all possibly infected sites when the patient does not seem to respond to the treatment. Some of the very irregular and seemingly incongruous results of therapy often reported in the literature may be due to inadequate study and consequent failure to recognize the intrusion and pathogenic significance of new strains.

Bone and Joint Changes in Leprosy. C. T. Kung, T. C. Chang, P. Y. Hsü and others. Chinese M. J. 79:130-137 (Aug.) 1959 [Peking].

The authors report on 55 patients with more advanced leprosy, who were selected from the Shanghai Municipal Leprosarium and in whom osseous changes occurred. Of the 55 patients, 32 had the lepromatous type of the disease, and 23 had the tuberculoid type. The bone and joint changes in these patients were classified as specific and nonspecific changes. The specific changes were due to direct invasion of the Mycobacterium leprae into the bone tissue and bone marrow cavity, and they occurred in 7 patients. In 5 of the 7 patients, these changes appeared as a small area of decreased density, with a hazy border and distortion or disappearance of the trabeculae, usually located in the metaphysis of the phalanges or metacarpus (pseudocystic formation). In the remaining 2 patients, change of expansion of the small tubular bone, with decrease in density, thinning of the cortex, and rarefaction of the trabeculae, was noted.

The nonspecific changes were subdivided into 7 groups: 1. Enlargement of the nutrient foramen was seen in 6 patients, 5 of whom had the lepromatous type of the disease. 2. Diffuse osteoporosis of various degrees was observed in all except 3 patients. 3. Absorption of the small bones of the hands and feet was the chief cause of mutilation of the extremities, these changes being observed in 75 hands and in 30 feet. In some patients, small bones were completely absorbed with loss of fingers and toes, but in others there was only atrophy of the soft tissue, the fingers and toes remaining intact. 4. Concentric absorption was observed in 26 patients, with the shaft itself and the marrow cavity of the small tubular bones gradually narrowed evenly, the ends being preserved. 5. Fractures were present in 7 patients, 5 of whom had chip fractures and 2 had fractures of the middle metatarsals, with fairly well-healed callus formation. 6. Secondary infections occurred, with formation of perforating trophic ulcers. 7. Small loose bony fragments were observed in the larger joints, such as the elbow, knee, and ankle, with some degree of subluxation similar to that of Charcot's joint. Suggestions made by the authors concerning the mechanism of the leprotic bone changes include neurotrophic changes of the osseous system and their acceleration by trauma and secondary infection.

RADIOLOGY

Simple Roentgenogram and Pulmonary Arterial Hypertension in Mitral Stenosis. R. Cruz, M. Besoain, S. Manubens and others. Rev. méd. Chile 87:617-623 (Aug.) 1959 (In Spanish) [Santiago].

The correlation between tensione values obtained by heart catheterization and the findings of chest roentgenography was studied in 37 patients with mitral or with mitral and tricuspid lesions. These patients were selected on 2 fundamental conditions, i. e., tensione measurements taken by heart catheterization and considered technically satisfactory, and at least one simple chest roentgenogram taken in frontal exposure and approximately at the same time as the cardiac catheterization. The types of lesions were pure mitral stenosis in 27 patients, mitral disease with predominance of stenosis in 2, mitral disease and tricuspid insufficiency in 6, and mitral stenosis with predominance of tricuspid insufficiency in 2. The systolic pressure of the pulmonary artery, obtained by catheterization in all 37 patients, was normal (up to 30 mm. Hg) in 5 patients, slightly increased (up to 40 mm.) in 10, mildly increased (up to 70 mm.) in 13, and markedly increased (over 70 mm.) in 9.

Comparative analysis of the roentgenographic and catheterization findings showed the following correlations. In 32 patients (86.5%) there was close parallelism between the roentgenogram and the catheterization findings, i. e., if the pressure was normal in the pulmonary artery, there were no arterial changes in the simple roentgenogram; if the pulmonary pressure was mildly elevated (up to 40 mm. Hg), there were some roentgenographic signs of arterial change; and if the pulmonary pressure was mildly or markedly elevated, the roentgenographic signs of arterial changes were always present. Only in 5 patients (13.5%) was there disagreement between the roentgenographic and the catheterization findings. [illegible] was manifest in patients with systolic hypertension (higher than 40 mm. Hg), who nevertheless were roentgenologically classified as grade 0. Kerley's lines were present in 12 patients, and always closely correlated with the degree of venous hypertension. Only in one patient did the presence of Kerley's lines coincide with a medium capillary pressure. These results indicate that in most cases the roentgenographic signs make it possible to diagnose, or at least to suspect, the existence of pulmonary arterial hypertension in mitral stenosis, by the roentgenographic signs of arterial changes (especially dilatation of the hilar and narrowing of the peripheral branches). The presence of Kerley's lines always means severe venous hypertension and is an indication for surgical treatment.

Routine Chest Roentgenograms: Fears and Practice. W. E. Boek, H. H. Shultz, G. D. Park and others. New York J. Med. 59:3403-3407 (Sept. 15) 1959 [New York].

In routine chest roentgenologic screening surveys, the benefits to be gained by the early discovery of intrathoracic disease must be weighed against the possible genetic hazards. Since all radiation effects may be cumulative, roentgen radiation exposure should be kept to a minimum, especially in younger persons. A chest roentgenogram, even a photofluorogram, affords a minute amount of radiation to the gonads when compared with certain abdominal and pelvic roentgenograms. However, since the radiation hazard associated with photofluorography is considerably higher than that from conventional chest roentgenograms, it is obligatory that photofluorographic roentgen-ray installations be properly shielded. Protective devices developed by the New York State Health Department's bureau of tuberculosis case finding consist of rectangular diaphragms which are placed over the tube outlet, 2.5 mm. of aluminum used for filtration of the x-rays, and protective lead aprons, suspended from the screen. These devices will cut down the gonadal dose from chest x-ray films with a minifilm unit from 5 to 0.4 mr. or a 12-fold reduction. The traditional large x-ray film units give an average gonadal dose of 0.25 mr.

In roentgenologic surveys in 2 counties, inquiries were made to learn how many of the 667 persons interviewed were worried about radiologic hazards. Nearly 9 out of 10 persons considered regular chest x-ray examinations very important, 9% were uncertain, and 3% were opposed. Although the fear of radiation harm was the most frequent reason given for their opinions by those uncertain or opposed to having regular chest x-ray films taken, it was not very important on an over-all basis. Altogether only 8% of the people were influenced by this concern.

Diaphragmatic Hernia in Infancy. J. O. Reed and E. F. Lang. Am. J. Roentgenol. 82:437-449 (Sept.) 1959 [Springfield, Ill.].

The authors report 48 infants with diaphragmatic hernia, who were classified according to diagnosis into 3 groups. The first and largest group consisted of 31 infants with pleuroperitoneal hernia; the second comprised 12 infants with esophageal hiatus hernia; and the third consisted of 5 infants with hernia involving the anteromedial or tendinous segment of the diaphragm. Pleuroperitoneal hernia is the commonest type of diaphragmatic hernia in infants and also the most dangerous one. In this series the left side was involved in 24 infants, and the right side in 7. The roentgenograms were almost always diagnostic. The roentgenologic findings were characteristic in almost all the infants, a mass being demonstrated in the lower one-half to two-thirds of the hemithorax; there were usually shown fluid levels in the intestinal loops in the thorax, displacement of the mediastinum to the opposite side of the chest, absence of a visible diaphragm on that side, an esophagus of normal length, and absence of intestinal gas in the abdomen. The latter finding might be significant if accompanied by absence of gas in the viscera contained in the chest.

If cardiorespiratory embarrassment is expected to increase with increasing distention of the stomach and intestine in the presence of large hernias, it is important in the neonatal period to delay feeding and to reduce the amount of swallowed air by gastric aspiration until the hernia has been repaired. Even very large defects in the diaphragm can be repaired in the newborn infant by an experienced surgeon. Of the 6 infants with pleuroperitoneal hernia who were not operated on, 5 died, as compared with 4 deaths among 25 infants in whom the hernias were reduced and the diaphragmatic defects repaired. Esophageal hiatus hernia was large and severe enough to cause respiratory distress in only 1 of the 12 infants in the second group. The third group of 5 infants with hernia involving the anteromedial aspect of the diaphragm had large eventrations which made diagnosis and treatment difficult.

Roentgen Therapy of Certain Complications of Acute Leukemia in Childhood. G. J. D'Angio, A. E. Evans and A. Mitus. Am. J. Roentgenol. 82:541-553 (Sept.) 1959 [Springfield, Ill.].

The control of secondary complications in children with acute leukemia has acquired greater importance because of the prolongation of life made possible since the introduction of antileukemic chemotherapy. Between 1953 and 1957, 372 children with acute leukemia, under the age of 14 years, were treated at the Children's Cancer Research Foundation of the Children's Medical Center, Boston. There were 199 boys and 173 girls. Children with an initial lymphosarcomatous phase were not included in this study. Ninety-five of the patients (55 boys and 40 girls) received roentgenotherapy for some secondary manifestations of their disease. Many of the remaining children had similar but less severe complications and did not require roentgenotherapy. All the children received chemotherapy throughout the course of their disease. There was no significant relation between the agent in use and the development of any of the complications; most of the complications appeared during hematological relapse, although some, particularly those involving the central nervous system, were manifested during remission.

The most favorable results with roentgenotherapy were obtained in patients with symptoms of the central nervous system and those related to the bones and joints. Satisfactory responses also were noted in patients with cutaneous and mucosal infiltrations and in those with miscellaneous leukemic masses. Hematuria was found to clear well in some children treated by this means. No untoward effects on the hematological status have been encountered in the patients so treated. However, not all the secondary difficulties of acute leukemia in childhood are helped by the use of irradiation. Most of the difficulties related to the abnormal clotting mechanism, which occur late in the disease, are not amenable to roentgenotherapy. Nevertheless, some complications which occur in children who are not in the terminal stage, regardless of whether they are in relapse or in remission, can be controlled satisfactorily by this management. The authors do not advocate indiscriminate use of irradiation each time a transient complaint develops, but when a disabling and persistent symptom appears, a trial of roentgenotherapy in small dosage is worthy of consideration.

Hyperparathyroidism, with Pseudoerosion of the Sella Turcica. J. Edeiken and W. Nagle. A. M. A. Arch. Int. Med. **104**:430-432 (Sept.) 1959 [Chicago].

The authors report on a 16-year-old girl with hyperparathyroidism and osteitis fibrosa cystica; there was an almost complete lack of visualization of the bony wall of the sella turcica associated with hyperparathyroidism resulting from a parathyroid adenoma. On admission to the Hospital of the University of Pennsylvania in Philadelphia, roentgenograms of the patient's skeleton showed a diffuse osteoporosis. Examination of the skull showed a diffuse demineralization of the bones of the cranium, with a "ground glass" appearance. There was a cystic lesion in the frontoparietal region on the left. The sella turcica could not be seen, and it was thought that a pituitary adenoma with marked enlargement and erosion due to an associated intrasellar tumor might be present. Glucose tolerance and blood sugar findings were normal, and the only suggestion of multiple adenomas was the appearance of the sella turcica. Chest roentgenograms revealed normal lung fields, but fluoroscopically there was displacement of the trachea and cervical esophagus to the right. This was thought to be due to a mass in the left lower lobe of the thyroid or left parathyroid.

The patient was operated on, and a parathyroid adenoma was removed from the left side of the neck. She did extremely well during the ensuing 2 months, and the roentgenograms of the bones revealed a rapid return to normal. It became apparent that the bony structures forming the sella turcica could not be seen previously because of marked demineralization, rather than erosion from a tumor. These bones rapidly remineralized and actually became relatively dense, when compared with the other bones of the cranium. Removal of a parathyroid adenoma thus permitted rapid remineralization of an otherwise normal sella turcica.

Roentgen Therapy of Intrathoracic Neoplasms. F. Buschke. California Med. **91**:134-136 (Sept.) 1959 [San Francisco].

Comparison of the results obtained in treating esophageal carcinoma by optimal surgical techniques with those obtained by the newest methods of radiation showed that the statistical results were similar. There was a 5-year salvage of about 3% of the patients by either operation or radiotherapy. More significantly, palliation was approximately the same by either method, as measured by survival of 41% through the first year, 15% through the second, and 10% through the third. The available data suggest that further technical improvements are not likely to produce any clinically significant advantage for either surgical management or radiotherapy of esophageal carcinoma. More good could be done for more patients by more careful selection of the treatment in each case, and also by avoiding post-therapeutic morbidity. The main considerations in selection of therapy are, in order of importance, the location in the esophagus, the nature of the tumor, and the patient's age. Usually the cause of failure is that metastatic deposits are already present in the paraesophageal and mediastinal lymph nodes by the time diagnosis is made. Control of these lymph nodes is impossible by either surgical treatment or by radiation therapy, but in about half of the patients adequate irradiation therapy will bring about palliation and will also lead to satisfactory reestablishment of esophageal function, with less morbidity than that produced by surgical operation.

Palliative roentgenotherapy has a definite, although limited, place in the treatment of bronchial carcinoma when applied with appropriate technique against certain symptoms. Anaplastic tumors can be controlled locally by irradiation, but because of their rapid dissemination radiotherapy should be aimed at the relief of pulmonary embarrassment caused by the rapid enlargement of mediastinal lymph nodes. Symptoms of bronchial obstruction can be reduced only by intense irradiation, but diffuse thoracic pain is more effectively palliated by sympathetic nerve block. It must be remembered that the purpose of therapy is not merely to prolong life but also to provide for the patient's comfort.

Leukemia in Children Exposed to Ionizing Radiation. R. Murray, P. Heckel and L. H. Hempelmann. New England J. Med. 261:585-589 (Sept. 17) 1959 [Boston].

Through the cooperation of all radiologists in Monroe County, New York, the authors obtained the names of 6,473 children to whom roentgen-ray treatments had been given since 1930. The list of treated children was checked against cancer files started in 1940 by the New York State Department of Health to provide an estimate of the frequency of leukemia among those exposed to ionizing radiation. In agreement with previous investigations, the incidence of leukemia was higher among irradiated than among nonirradiated children. A greater than expected number of deaths from leukemia occurred not only among children treated for an enlarged thymus but also among those treated for pertussis and lymphoid hyperplasia.

Conversely, a retrospective study of children with leukemia in Monroe County was conducted to determine prenatal and postnatal exposure to ionizing radiation by a questionnaire-type interview with the parents of 75 children dying of leukemia in this county between 1940 and 1957. Interviews were obtained in the case of 65 of the 75 children. The results of this study indicated that exposure of children with leukemia to the x-ray sources investigated, versus the exposure of matched deceased controls and living siblings, was higher only for so-called deep x-ray therapy. Prenatal exposure was not found to be high in the small sample of patients with leukemia. Siblings of children with leukemia were found to have the highest [illegible] of fetal irradiation and postnatal [illegible]

ANESTHESIA

Changes in Blood Pressure and Pulse Rate During Fluothane Anesthesia: A Comparative Clinical Study. J. Moyers and C. B. Pittinger. Anesthesiology 20:605-607 (Sept.-Oct.) 1959 [Philadelphia].

Some reports on anesthesia with halothane (Fluothane) had given the impression that hypotension and bradycardia are more frequent and severe with this agent than with others commonly used. The authors challenged this impression by making a comparative study of blood pressure and pulse rate in patients anesthetized for surgical procedures requiring abdominal relaxation. Cyclopropane, ether, nitrous oxide, and Fluothane were the primary anesthetic agents. For each of the 4 agents studied, 50 anesthesia records were taken at random from departmental files for the year 1957. There were selected only those records which were made during the course of anesthesia for intraperitoneal surgical procedures requiring abdominal relaxation. A variety of gynecologic, urologic, and general surgical procedures was represented. The operations lasted from half an hour to 6½ hours.

Anesthetists were usually residents-in-training who did not employ specific Fluothane vaporizors. The average systolic pressure during Fluothane anesthesia was 11.7% lower than the average preanesthetic value. This degree of hypotension was not significantly greater than that observed during ether anesthesia. Furthermore, extreme hypotension, however brief, was no more common or severe with Fluothane than with cyclopropane, ether, or nitrous oxide. Bradycardia need not be identified with Fluothane anesthesia during surgery.

Fat Embolic Phenomena During Anesthesia and Surgery. J. O. Cale, C. F. Gregory and M. T. Jenkins. Texas J. Med. 55:756-759 (Sept.) 1959 [Austin].

This is a preliminary report on studies carried out to investigate the presence of circulating fat particles in the blood of patients undergoing elective orthopedic procedures and in some patients having sustained trauma prior to operation. The study was designed to indicate also the results of various anesthetic agents and techniques. For the most part the patients studied were those having operations on the lower extremities. Blood samples were obtained from near the site of the injury or surgery whenever possible. In the majority of cases, the blood samples were obtained from the inferior vena cava by means of an indwelling polyethylene catheter introduced through the contralateral femoral vein. Urine samples were obtained by means of an indwelling catheter introduced without lubricant. A record of the patient's physiological status and blood and urine samples were obtained at appropriate intervals before anesthesia, after induction of general anesthesia, or after the development of spinal anesthesia, before and immediately after surgical manipulations, in the immediate postoperative period, and 24 and 48 hours postoperatively.

In this small initial series of 100 patients, the clinical picture of fat embolism did not occur, but hyperchylomicronemia was frequent. In 54 of the patients there was a significant display of circulating chylomicrons without evidence of physiological changes. In the study of individual protocols it came to be expected that patients with liver disease or a history of alcoholism would have fat in significant particle size and quantity during any operative procedure. Five patients with cirrhosis of the liver displayed the greatest increase in chylomicron content. The application of a tourniquet to the extremity to be operated on prevented an increase in the circulating chylomicrons, but upon release of the tourniquet a shower of chylomicrons was demonstrated. None of the patients experienced shock during the surgical procedures, which eliminated this possible potentiating factor of fat embolism.

There were a number of patients in whom the complete picture of fat embolism should have developed, if it could be produced by only large quantity and size of chylomicrons. Failure of this to occur suggests that additional factors are necessary. The possible role of blood lipase in the pathogenesis of traumatic fat emboli is mentioned. A small amount of free fat may be liberated from the bone marrow at a fracture site; although in itself not lethal, in certain sensitive persons this process may stimulate the production of an excess amount of blood lipase, which, in turn, not only hydrolyzes the fat liberated from the fracture site but also breaks down body depot fat, which may then be carried to the pulmonary or cerebrovascular beds. In this series 12 patients with a significant increase in circulating chylomicrons showed no increase in lipase. Anesthesia per se probably plays a minor role in the pathogenesis of fat embolism, although the fat solvent anesthetic agents especially are related to hyperchylomicronemia. No anesthetic agent or technique seems to be contraindicated, solely because of fear of fat embolism.

BIOCHEMISTRY

Antibiotic Sensitivities of Staphylococci Isolated Before and After Patients Were Given Antibiotics. B. A. Waisbren and C. L. Strelitzer. Am. J. M. Sc. 238:202-210 (Aug.) 1959 [Philadelphia].

This study was undertaken to answer the question: Does the administration of an antibiotic to a patient cause a change in the antibiotic sensitivity of the staphylococci that are infecting that patient? Data for the answer were obtained by comparing the antibiotic sensitivity of staphylococci that were isolated from 50 patients before and after they were given the antibiotics to determine what, if any, changes in sensitivity had occurred. Bacterial sensitivity tests made before and after antibiotic administration were available in 152 instances. The sensitivity of staphylococci to the antibiotic administered was unchanged in 53 instances, increased in 42, and diminished in 57. Attempts to prevent the development of antibiotic resistance by giving combinations of antibiotics were ineffectual.

These findings show the inadvisability of any statement regarding a general effect of the administration of antibiotics on antibiotic sensitivity of staphylococci. Perhaps the most important point emphasized by the rather limited data in this study is the apparent absence of an a priori relationship between the administration of an antibiotic to a patient and the subsequent isolation of staphylococci resistant to antibiotics from that patient. Influences other than the use of antibiotics must, therefore, be sought to explain the changing resistances of staphylococci to antibiotics. A simple explanation unrelated to the use of antibiotics may lie in the natural variability of the Staphylococcus species, to which its ubiquitous position in the world of bacteria is attributable. This same natural variability would also account for the fact that drugs selected on the basis of a particular biochemical characteristic will always eventually become obsolete, because the biochemical characteristic concerned will change in accordance with the inevitable changes in the biochemical nature of the staphylococci.

Isolation of Cortisol from a Pheochromocytoma. P. J. Mulrow, G. L. Cohn and R. Yesner. Yale J. Biol. & Med. 31:363-372 (June) 1959 [New Haven, Conn.].

The authors report on a 62-year-old woman who was admitted to the memorial unit of the Grace-New Haven Community Hospital for surgical removal of a 169-Gm. adrenal tumor, but had none of the signs or symptoms of an adrenocortical or medullary tumor. On microscopic examination of the surgical specimen, the tumor resembled a pheochromocytoma, yet contained vacuolated tumor cells suggestive of lipid. Assay of the tumor revealed an excess of catechol amines. Slices of tumor tissue released a compound in vitro which had the chromatographic characteristics of the standard compound F (cortisol). There are reports in the literature which indicate that pheochromocytomas may also secrete adrenocortical steroids. The clinical picture would depend on the type and quantity of steroid produced. Perhaps part of the circulatory collapse sometimes following surgical removal of a pheochromocytoma may be due to removal of a steroid-producing tumor. This tumor might be producing a quantity of steroid sufficient to inhibit corticotropin (ACTH) secretion, yet insufficient to produce symptoms of hyperadrenalism. The removal of this tumor would leave atrophied adrenals to cope with the stress of the surgical intervention. This did not appear to be the situation in this patient, since her postoperative precipitous drop in blood pressure did not respond to hydrocortisone alone, and she had to be on maintenance therapy with levarterenol (Levophed) bitartrate. Actually, the nature of the vascular collapse was unclear. Such a clinical state would be difficult to detect before the surgical intervention. In vitro studies would help to clarify this possibility.

Gluten-Induced Enteropathy: The Effect of Partially Digested Gluten. A. C. Frazer, R. F. Fletcher, C. A. C. Ross and others. Lancet 2:252-255 (Sept. 5) 1959 [London].

Intolerance to wheat gluten is a major factor in the etiology of the enteropathy observed in almost all children with celiac disease and most adults with idiopathic steatorrhea. Treatment with a gluten-free diet has a beneficial effect in such patients; reintroduction of gluten is deleterious. The authors attempted to determine whether the harmful effect of wheat gluten in patients with gluten-induced enteropathy was modified by digestion of the gluten with pepsin and trypsin. The digestion stopped short of complete hydrolysis, and the resultant products were tested in gluten-intolerant patients. The wheat gluten used for the studies had not been treated by additives or improvers, and the results obtained show that the chemical treatment of flour is not a factor in producing deleterious effects in patients with gluten-induced enteropathy. Enzymic degradation of gluten by pepsin and trypsin in vitro, with or without subsequent precipitation of residual protein by autoclaving, did not materially alter the deleterious effect of gluten in these patients. The harmful effect of the gluten must be due to the presence of a peptide or some other fragment in wheat gluten, which is not handled as effectively by patients with gluten-induced enteropathy as by normal people.

Studies were made on gluten fractions, and it was found that the water-soluble product (fraction 3) contained 66% ultrafiltrable material and 8% free amino acids. This was autoclaved to yield fraction 3A. Gluten and fraction 3 had antigenic properties, giving a positive response in isolated intestine from guinea pigs sensitized to wheat gluten; fraction 3A was negative when similarly tested. Fractions 3 and 3A were tested in patients with gluten-induced enteropathy. They were equally deleterious, and did not appear to be less toxic than the gluten from which they were derived. The possibility that breakdown products of gluten may have antigenic properties is still being studied.

PUBLIC HEALTH

Poliovirus Antibody Response After Various Vaccination Schedules and at Different Ages. D. R. E. MacLeod, C. W. J. Armstrong, G. W. O. Moss and others. Canad. M. A. J. 81:443-449 (Sept. 15) 1959 [Toronto].

The authors investigated the antibody response to poliomyelitis vaccine in infants, in children, and in adults. A good response was seen in children and adults after the first 2 injections of poliomyelitis vaccine. After the booster dose all children, including those initially without antibody of specific type, produced antibodies for all 3 types of poliomyelitis virus. Satisfactory antibody levels were present in children, ranging in age from 8 to 9 years, 18 months after the booster dose. There seems to be so far no evidence that maintenance of immunity by means of Salk-type vaccine will present problems very different from those presented by other antigens. Two injections of the vaccine, when spaced 4 weeks or more apart, produced a higher antibody level than one injection. The response to a second dose, when given from 7 to 10 months after the first dose, was as good as when the dose was given one month after the first injection. Observations made by other workers indicate even better results. This shows that, if a delay occurs in giving the second dose, the inoculations may be continued regardless of the interruption. Three doses of poliomyelitis vaccine, given within a period of 4 weeks, did not produce higher antibody levels than 2 doses. There was, however, a certain increase in immunity when the 3 injections were given within a period of 2 months. The observed reactions were consistent with the concept that the secondary phase of reaction begins within 4 weeks and increases considerably during the second month after the primary stimulus.

The time needed to reach the maximum development has not been established, but it is possible that it varies according to the antigen, the number of doses, the age of the patient, and other factors. It is recommended that the second dose be given not less—preferably even more—than 4 weeks after the second, but certainly before the next poliomyelitis season. The reaction to vaccination was not so good in infants, aged 3 to 12 months, as in older children, but the difference was not significant. There are probably 2 or 3 factors that are responsible for this difference, namely, sensitization due to previous infection, maternal antibody, and the age of the infant. Prior sensitization which increases the response to vaccine was found in a higher proportion of children than of infants. High levels of maternal antibody diminished the reaction in some infants. Certain factors affecting growth may also play a part, but any difference due to age between infants of 3 months or more and older children is very small. Low levels of maternal antibody do not inhibit the reaction. Most of the infants, 3 months or more of age, had a satisfactory response after 3 doses of vaccine given one month apart.

BOOK REVIEWS

Mazer & Israel's Diagnosis and Treatment of Menstrual Disorders and Sterility. By S. Leon Israel, M.D., Professor of Gynecology and Obstetrics, Graduate School of Medicine, University of Pennsylvania, Philadelphia. Fourth edition. Cloth. $15. Pp. 666, with 147 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1959.

This book, which is practically a new one, was prepared by Israel alone. It is much larger than the third edition by Mazer and Israel and contains many more illustrations. The number of changes made and the amount of new data included indicate the magnitude of the author's task in bringing this book up to date. Every aspect of menstrual disorders and sterility is covered thoroughly. The advice given regarding therapy is specific, so that every general practitioner should find this book useful in his daily practice. There is an excellent chapter entitled The Male Factor in Barren Marriages, by Charles W. Charny. Because of the present controversy concerning the possible harmful effects of irradiation on young women and children an important chart entitled Clinical Argument For and Genetic Reply Against Low-Dosage Irradiation of the Ovaries is included. Contrary to Israel's previous belief and practice he now says, "When serious-minded scientists of an atomic age the world over issue recommendations aimed to decrease the hazards of ionizing radiation to future generations of mankind one cannot help but be persuaded morally not to employ low-dosage gonadal irradiation." The book is lucidly written; the amount of valuable information given is enormous; and the illustrations are numerous, clear, and instructive. The paper is sturdy, the book is well bound, and the price is fair. The popularity of the book should greatly increase with this fourth edition.

Anatomy of the Human Body. By Henry Gray, F.R.S. Edited by Charles Mayo Goss, M.D., Professor of Anatomy, Louisiana State University School of Medicine, New Orleans. Twenty-seventh edition [American centennial]. Cloth. $17.50. Pp. 1458, with 1174 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1959.

This centennial edition of a famous textbook is shorter (1458 pages compared to 1480) than the previous edition. The section on the nervous system, in particular, has been drastically revised. A number of new illustrations have been inserted, but many old ones have been taken out so that the total number is less (1,174 compared to 1,202). With the new illustrations some errors have crept in (corpus mamillarius for c. mamillarium, page 878; foramen interventricularis for f. interventriculare, and chiasma optica for c. opticum, page 880). Among the old retained figures errors can also be found (ductili transversii for ductuli transversi and Falloppii for Fallopii, page 1374). Other proper names, both historic and contemporary, are mutilated at times. Magendie fares the worst. His name is misspelled in the index (page 1435), in the text (868), and in the legend to fig. 732. On page 1041 appears an antique figure that has surely caused vexation if not vertigo in countless long-suffering medical students; the labels in half of the figure, which must be read with the book held sidewise, are to be compared with the labels in the other half, which must be read with the book turned through 180 degrees. The index abounds in small errors like fossa navicularis uretha for f. n. urethrae, tuberculum majur for t. majus, and vasa aberrans for vas aberrans or vasa aberrantia. Eponymic phrases have not been eliminated, and it is puzzling to read the recommendation (page 1307) that the term "ampula of Vater" (sic) be discarded in favor of the "papilla of Vater." It is also strange to find the density of bone stated in pounds per cubic foot and strength in pounds per square inch (page 310). The use of these units is hard to justify by either scientific or practical considerations in the present context.

This work deserves the respect that is generally accorded to so large a mass of material so diligently assembled, but one must assume that the superficial errors noted may be matched by others less easily detected. It is traditional for lawyers to embarrass medical witnesses by referring to Gray's Anatomy as a supreme authority. To any physician who finds himself in that situation, and to the medical student who has deviated from "Gray" in an examination paper, the details cited above may be welcome as proof that neither the original author nor the train of editors who have succeeded him have been infallible.

Report on the National Conference on the Legal Environment of Medical Science, May 27-28, 1959. Sponsored by National Society for Medical Research and University of Chicago. Paper. Pp. 114. National Society for Medical Research, 920 S. Michigan Ave., Chicago 5, 1959.

The activities of antivivisectists have focused attention on the care of laboratory animals and the responsibilities of research workers with respect to experiments on animals. Recent developments, making possible the transfer of parts of

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

one human body to another and the preservation of such parts in "banks," have provoked a growing interest in organ transplants and autopsy procedures. Over and above all this run increasing doubts and uncertainties as to the legal and ethical aspects of the whole problem of human and animal experimentation. For a number of years the National Society for Medical Research has studied these questions. One outgrowth of this interest was the conference here reported, which was held last under the joint sponsorship of the society and the University of Chicago. The deliberations were organized into sessions on the use of cadavers, organ transplants, and autopsy procedures; the care and use of laboratory animals; and legal and ethical aspects of clinical research. The chairmen of the sessions were, respectively, Dr. Russell T. Woodburne, department of anatomy, University of Michigan; Dr. William T. S. Thorp, dean of the college of veterinary medicine, University of Minnesota; and Rev. Thomas J. O'Donnell, regent of the college of medicine, Georgetown University.

This report contains the introductory remarks of Dr. Lester Dragstedt, conference chairman, and of the session chairmen. It includes the papers presented in each session and the conclusions of a number of special committees appointed in the course of the conference. An idea of the general scope and interests of the participants may be gained from the random listing of a few of the items presented. These include consent for autopsies, anatomical materials and anatomical laws, legal and ethical factors regarding animal experimentation, medical research on human beings, Nuremberg code, and legal battery and clinical research. Concluding the report is an extensive bibliography. The report is the most complete and current discussion of the factors included in the legal environment of medical research that may be found today. It should be of great value to the research workers and to the practicing physician, who is sometimes troubled by the possible legal consequences of using new medicaments and techniques in treating his private patients.

Handbook of Physiology: A Critical Comprehensive Presentation of Physiological Knowledge and Concepts. Section 1: Neurophysiology. Volume I. Editor-in-chief: John Field. Section editor: H. W. Magoun. Executive editor: Victor E. Hall. Cloth. $22. Pp. 779, with illustrations. [Published for] American Physiological Society, Washington, D. C., by Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1959.

This volume is a landmark in American scientific publishing, for it initiates the first effort in this country to present comprehensively the entire substance of a basic medical science in hard covers. Two subsequent volumes will complete the section on neurophysiology. This section opens with a history of neurophysiology, which is followed by subsections on neuron physiology, brain potentials and rhythms, sensory mechanisms, and vision. Although the book is addressed primarily to professional physiologists, most chapters require no more than a sound general knowledge of the nervous system to be readily understood. The work, therefore, has great interest for both clinicians and nonphysiologists working in allied neurological fields. Clinicians should be particularly interested in the sections on epilepsy and pain where the orientation to human disease is clear.

The contributors and editor have addressed themselves well to the difficult task of achieving balance and have prepared chapters which are complete, analytical, and authoritative and which provide the subject's enduring fundamental background as well as presenting recent important advances. The great disadvantage of compendiums of this type is that, despite their expense and detail, they rapidly become outdated. To a degree, this risk has been minimized in the present work by developing most of the topics in historical perspective, thereby showing the growth of ideas about the subject as well as the most recent pertinent experimental results. The editing is superior so that the subject matter generally is tied together in orderly progression despite the fact that each chapter is presented by a different worker having internationally recognized competence in the field. The printing and illustrations are clear, and the proof-reading has been excellent. If future volumes meet the high standards set by this one, many physicians should want at least the individual sections of this handbook in their personal libraries.

Brucellosis in the USSR: A Review of the Literature. By Julian Hoptman. U. S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health. Public Health Service publication no. 635. Paper. 30 cents. Pp. 77. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1959.

Before World War II the Russians recognized that brucellosis was a serious economic and public health problem throughout the USSR. Although great strides have been made in controlling the disease, brucellosis is still considered the most important zoonotic disease in that country. The author of this monograph has performed a first-rate service in reviewing the literature and presenting the problem of brucellosis in the USSR. The magnitude of the problem is formidable. Brucellosis in Russia is primarily a disease of sheep and goats, and almost unbelievable numbers of human beings from various areas have become infected with Brucella melitensis. For the most part, human brucellosis is an occupational disease involving livestock producers, veterinarians, farmers, and those working in packing plants. This pattern is found elsewhere in the world.

Perhaps the most revealing aspects of this study are the aggressive methods used for controlling the disease in man and in animals. More than two million human beings have been immunized with a living vaccine composed of Brucella abortus strain 19. This is the strain used to immunize cattle in the United States. The Russians have claimed that this procedure has reduced the incidence of human illness markedly. Little information is presented concerning the potential dangers of using this living vaccine in human beings. Russian investigators appear to be carrying out basic studies on the causative organisms and on the pathogenesis of the disease. Of particular interest are the efforts (partially successful) to isolate a brucella bacteriophage. This book should be of special interest to students of this disease and to public health workers. It demonstrates once again that various countries have health problems in common and that interchange of information can be beneficial to all.

Steroids. By Louis F. Fieser, Sheldon Emery Professor of Organic Chemistry, Harvard University, Cambridge, Mass., and Mary Fieser, Research Fellow in Chemistry, Harvard University. Cloth. $18. Pp. 945, with illustrations. Reinhold Publishing Corporation, 430 Park Ave., New York 22; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, England, 1959.

This book may be considered the fourth edition of the book formerly entitled "Natural Products Related To Phenanthrene." The latest edition appeared in 1949 and was somewhat broader in scope than the present edition inasmuch as it contained short chapters on morphine alkaloids and resin acids in addition to a thorough treatment of the steroids. The latter material has been completely reorganized and revised and information from literature appearing as recently as 1959 has been included. The present volume gives a complete discussion of steroids from the chemical point of view. The authors deal with such subjects as discovery and isolation, determination of structure and configuration, chemical synthesis and biosynthesis, and the chemical reactions and physical characterizations of such compounds or classes of compounds as cholesterol, the D vitamins, vegetable sterols, bile acids, estrogens, androgens, homosteroids and norsteroids, adrenocortical hormones, cardiac active principles, sapogenins, and alkaloids.

The volume should be of particular value to those interested in the organic chemistry of steroids because of the thoroughness with which the authors discuss the various types of reactions used in elucidating the structure of synthesized steroids. The new edition is timely because of the great increase in the use of steroids in medicine. The book contains a glossary which explains the abbreviations, symbols, and nomenclature used in the book. It is supplied throughout with appropriate references and contains both author and subject indexes.

1846-1958 Digest of Official Actions, American Medical Asociation. F. J. L. Blasingame, M.D., Executive Vice President. Cloth. $5. Pp. 779. American Medical Association, 535 N. Dearborn St., Chicago 10, 1959.

This publication presents for the first time a digest of official actions arranged in the form of an encyclopedia. As indicated in the introduction, "The subject matter is divided into broad classifications to present an overview of each subject. Supplementing the body of the work is a detailed index which points to specific items or subclassifications. Thus, a historical continuity is preserved and, at the same time, quick reference to individual events is made possible." This volume is absolutely vital to those who wish to study or review actions of the American Medical Association since its establishment. The House of Delegates is the final policy making body of the Association. This volume makes it possible to review the history of the attitude of the Association on any subject on which it has ever taken a position. It is intended that supplemental volumes will be published every five years so that it will be possible for readers to be informed about the current policies of the A. M. A. This book, in short, is an invaluable reference source of information about the American Medical Association.

Before You Marry. By Sylvanus M. Duvall. [Second edition of 101 Questions to Ask Yourself before You Marry.] Cloth. $3.50. Pp. 252. Association Press, 291 Broadway, New York 7, 1959.

This is a simply-written and practical book which can be recommended by physicians to young people about to be married. It deals in simple, sensible, and practical terms with such questions as the chances for success in marriage; how does one know it's love; fact and fiction about sex; practical everyday aspects of marriage, such as finance, personality adjustment, mental health, and character of the proposed spouse; and "Who Is Right for You?" There is a good chapter on mixed marriages dealing not only with religious differences but with social, educational, and racial differences as well. "The Family You Marry" is dealt with realistically. There are chapters on emergencies and crises and how best to bind the marriage into permanency. There is a useful bibliography, in general at the college level.

The Modern Family Health Guide. Edited by Morris Fishbein. Contributing specialists: Harry Bakwin and others. Cloth. $7.50. Pp. 1001, with illustrations. Doubleday & Company, Inc., Garden City, N. Y.; 575 Madison Ave., New York 22, 1959.

As the editor states, this two-section volume has been carefully tailored to meet the needs of the average reader. The first section deals with modern concepts of health and disease. The second, identified as alphabetical or encyclopedic, contains thousands of brief discussions of a great variety of topics such as medical terms, many minor and major illnesses, commonly-used remedies, and nursing practices. The discussions in the first part were contributed by 26 recognized authorities. The editor himself is responsible for a chapter on body function and another on respiratory diseases. Pneumonia, however, is treated separately in the alphabetical section.

Part 2 contains material on infancy, childhood, and adolescence. Diseases of the heart, digestive system, and nervous system occupy other special sections, and there are discussions of first aid, the problem of geriatrics, medical statistics, and various major diseases.

An extensive index adds to the usefulness of this practical volume. Although there are relatively few illustrations, tables abound. There is a detailed chart of diseases, showing cause, symptoms, immunization, and treatment. The section dealing with the digestive system contains a wealth of information about special diets. The nonmedical browser or anyone with some specific curiosity to satisfy should find this book of great interest. Care has been taken to provide cross references from material in the encyclopedic section to the general discussions in the first portion of the book.

First Report on the World Health Situation 1954-1956. Official records of World Health Organization no. 94. Paper. $3.25; 17s. 6d.; 10 Swiss francs. Pp. 392, with illustrations. World Health Organization, Palais des nations, Geneva, Switzerland; Columbia University Press, International Documents Service, 2960 Broadway, New York 27, 1959.

In this report the influences affecting the health of peoples are discussed, as is the state of the public health in the world at large. The first part of the report is a general survey of conditions on a world-wide basis. Part 2 consists of reviews of their own health conditions by representatives of the various nations participating in the World Health Organization. As a source of official information, this volume should be highly useful to public health staffs, statisticians, sociologists, diplomats, and others interested in health as a factor in world economy, politics, and peace. Although WHO has been functioning for a number of years, this volume is the first report of the world health situation, and it covers the years 1954 to 1956. The lag in international information gathering and compilation is even greater than that to which we are accustomed in the United States.

Planning Homes for the Aged. Geneva Mathiasen, Executive Secretary, National Committee on Aging, National Social Welfare Assembly, New York, and Edward H. Noakes, editors. Cloth. $12.75. Pp. 119, with illustrations. F. W. Dodge Corporation, 119 W. 40th St., New York 18, 1959.

A study of the content of this book suggests that the title might better have been "Planning an Institution or Dormitory to Provide Housing and Sheltered Care for the Aged." The objective of all the contributors was to combine multiple housing with some degree of medical care for the residents. It was realized by one of the contributors that "as the number of residents in each unit increases, the possibility of retaining a homelike atmosphere decreases." The statement that the group aged 65 years and over is increasing at the rate of 2,000 a day is not substantiated by information from the Department of Health, Education, and Welfare. There is no doubt that the need for this type of an institution will vary in different parts of the country, but a nation-wide urgency is not proved. There is a great deal of repetition in discussion of the location of the housing in relation to libraries, transportation, shopping centers, medical care, and factory sites. Plans outlined include such facilities as doctors' and dentists' offices; laboratories for routine blood and urinalysis, electrocardiography, basal metabolism, and x-ray studies; and ear, nose, and throat examining rooms. This type of construction would be within the framework of nursing home regulations in most states. There is a question of whether the need for this type of service would warrant the expense in space and equipment. At present there is difficulty in the classification of nursing homes, and this book seems to be a contribution in this field rather than in the area of housing for elderly persons who are well. The needs of the majority of those older than 65 years has not been covered in this work.

Teaching Comprehensive Medical Care: A Psychological Study of a Change in Medical Education. By Kenneth R. Hammond, and Fred Kern, Jr., M.D., and others. Study jointly conducted by members of staffs of Behavior Research Laboratory and School of Medicine of University of Colorado. Cloth. $10. Pp. 642, with illustrations. Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass.; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, England, 1959.

This volume presents an interesting and valuable portrayal of the program for teaching of comprehensive medical care initiated by the University of Colorado School of Medicine in 1953. The joint study associated with the project involved the Behavior Research Laboratory and the School of Medicine of the University of Colorado so that the experiment could be adequately evaluated as it was being conducted. The volume is presented in sections dealing with the educational program, the research program, methodology, findings and conclusions, special studies, and appendixes. The section presenting findings and conclusions offers particularly valuable reading for those concerned with medical education and practice in the modern setting. This portion of the volume discusses the findings of the project concerning students' acquisition of medical, psychological, and sociologic knowledge, skill, and attitudes. There is a wealth of carefully presented information as to the comparative value of the general medical clinic experience and other facets of students' introduction to the concept of comprehensive medical care. The comparison of the effects of the two studies analyzing the results of the experience in the general medical clinic versus the regular course of study merits careful study, for it highlights the factors that determine the values of such programs. This volume is a significant contribution to medical education.

QUESTIONS AND ANSWERS

PARA-AMINOBENZOIC ACID

To the Editor:—*Is para-aminobenzoic acid harmful (carcinogenic) or beneficial?*

R. P. Little, M.D., Davos-Platz, Switzerland.

Answer.—There is no evidence that para-aminobenzoic acid (PABA) is harmful or carcinogenic. Many workers include PABA among the B-group of vitamins, while others consider it a microbial nutrilite, since it has not been shown to be required by man and other higher animals. PABA is found in such natural plant and animal materials as cereal grains, yeast, eggs, milk, and meats. Detectable amounts are normally present in human blood, spinal fluid, urine, and sweat. PABA is a component of several biologically important systems, including those involving folic and folinic acid. It may not be possible to say that dietary PABA is directly beneficial to man, but there are indirect beneficial aspects of the substance through its participation in a number of fundamental biological processes.

In recent years, PABA, especially in the form of its potassium salt (Potaba), has been used clinically extensively and at high dosage levels. Its beneficial effects first were demonstrated in typhus and other rickettsial infections. When administered in a 12-Gm. total, daily dosage, Potaba was shown to be beneficial in scleroderma, Peyronie's syndrome, posttraumatic and postburn scars, certain forms of pulmonary fibrosis, and other disorders associated with excessive fibrosis. Larger doses have been administered to patients with bullous disorders and generalized, nonsuppurative inflammatory processes of the skin. Some patients have taken continuously 12 to 18 Gm. daily of the compound for as long as a decade. Side-effects such as anorexia, nausea, fever, and rash have occurred infrequently and subside with omission of the drug. Desensitization can be accomplished and treatment resumed. Leukopenia is a rare, secondary complication. Hypoglycemia can result from taking large amounts of PABA without adequate caloric intake and should be prevented by dietary control.

The judicious use of pharmacological doses of PABA (as Potaba) may be beneficial in a number of poorly understood disorders. In long-term therapeutic experiences, there has been no evidence of carcinogenicity of the compound.

References

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2. Williams, R. J.; Eakin, R. E.; Beerstecher, E., Jr.; and Shive, W.: Biochemistry of B Vitamins, New York, Reinhold Publishing Corporation, 1950.
3. Zarafonetis, C. J. D.: Treatment of Scleroderma, Ann. Int. Med. **50**:343-365 (Feb.) 1959.
4. Zarafonetis, C. J. D.; Curtis, A. C.; and Shaw, J. M.: Treatment of Pemphigus with Potassium Paraaminobenzoate, Am. J. M. Sc. **231**:30-50 (Jan.) 1956.

BIOPSY OF CERVIX AND ELECTROCAUTERY

To the Editor:—*What are the relative merits of "cold coning" of the cervix for biopsy versus electrocautery and electrocoagulation, in terms of surgical benefits for the patient? Does this method give the pathologist a better specimen for diagnostic study?* *M.D., California.*

Answer.—From the pathological standpoint, a better specimen is obtained by cold coning, for there is no disturbance of cell structure, whereas cell distortion and destruction is caused by electrocautery and electrocoagulation. The surgical benefits obtained by the patient from each procedure can be the same, provided adequate excision is done.

If there is a suspicious or positive Papanicolaou stain, the endometrial cavity and the endocervix should be fractionally curetted and the specimens kept separate. If a topographic-histological study of the cone is to be done, the endocervix should not be curetted.

IRRADIATION OF THYMUS

To the Editor:—*The comments on irradiation of the thymus,* The Journal, *Aug. 29, page 2264, and its relation to thyroid malignancy reflect accurately the current opinion concerning the possible harmful effects from irradiation during the childhood years. Another important aspect of this problem relates to the leukemogenic potentialities of radiation. In "Leukemia and Medical Radiation," which concerns itself with a study of 251 leukemic children (Pediatrics 23:453 [March] 1959), Polhemus and Koch state "exposure to radiation was significantly more frequent among the leukemic group" as compared with an equal number of matched controls. It also was*

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

noted that "thymic irradiation was found to be associated with six times the usual incidence of leukemia." Such reports should alert the practitioner to weigh carefully his recommendations for thymic irradiation therapy.

George X. Trimble, M.D.
Seaside Memorial Hospital
Long Beach, Calif.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Too often there is a tendency to magnify adverse occurrences in medicine without adequate proof. When one draws conclusions from reports involving specially selected groups and then generalizes from these conclusions, the interpretations are not properly definitive. Polhemus and Koch noted in their survey of 251 grouped leukemic children, gathered from different environments, that only 12 developed leukemia subsequent to irradiation administered at one time or another in their lifetime. A similar survey of 251 children, who were apparently normal and had never received irradiation, showed that 2 developed leukemia. Of the leukemic group of 251 children 32 had relatives with leukemia, while only 6 in the control group were so involved. Might not this familial involvement play an important role in the incidence of leukemia? Roentgen rays are known to have antileukemic therapeutic properties and the children who subsequently developed leukemia did so despite x-ray therapy rather than because of it. Dameshek* (J. A. M. A. 163:838 *[March 9] 1957) stated, "It must be admitted that even in heavily irradiated individuals, the occurrence of leukemia is relatively uncommon. . . . It is certainly by no means proved that the various diagnostic and therapeutic procedures are clearly related to human beings, nor is it clear how such exposure might lead to leukemia." When a child's life is endangered by a persistently enlarging thymus, and since we know by experience that irradiation is lifesaving, such therapy is indicated. Irradiation, properly administered over the short time required by this emergency situation, will do no harm.*

CONVULSIVE SEIZURES

To the Editor:—*In* The Journal, *Sept. 26, page 498, there was the history of a 42-year-old man who had two convulsive seizures occurring two years apart. The electroencephalographic tracing was normal. The answer indicated that the patient probably had a convulsive seizure "of the usual sort, the etiology of which is often obscure." This answer ignores one of the most important maxims in neurology: an adult, who has a convulsive seizure and a history of not having previous seizures, must have further neurological evaluation for diagnosis of a brain tumor.*

Richard J. Brzustowicz, M.D.
277 Alexander St.
Rochester, N. Y.

MALIGNANT ERYTHROCYTOSIS

To the Editor:—*In answer to the question about the treatment of malignant erythrocytosis in* The Journal, *Oct. 3, page 632, the consultant stated that there was no known treatment and that of the agents used to treat a patient with leukemia none has been effective in malignant erythrocytosis. In my experience this is not correct. On occasion I have had a dramatic hematological response from therapy with large doses of corticosteroids and the antimetabolite, 6-mercaptopurine.*

Freeman M. Wilner, M.D.
15001 W. Eight Mile Rd.
Detroit 35.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*As pointed out by Dameshek and Gunz in "Leukemia" (London, Grune & Stratton, Inc., 1958, pp. 279-280), the Di Guglielmo syndrome not infrequently is just a phase of leukemia; that is, if the patient lives long enough the picture becomes leukemic. When such a situation exists, antimetabolites and steroids may be of some value. When the disease is in the pure erythroblastic phase, the opinion of most workers is that therapy has no effect.*

BLOOD-TINGED SEMEN

To the Editor:—*In* The Journal, *Sept. 16, page 496, the urologist who answered the question on blood-tinged semen gave a good résumé and described treatment, but he did not advise cystoscopy, which is essential to determination of the origin of blood in the urinary tract. In one patient hemospermia was found to be due to a bladder neoplasm which had been pulled into the posterior urethra during ejaculation.*

Harry Bergman, M.D.
1749 Grand Concourse
Lewis Morris Building
New York 53.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*It was an error not to mention that these patients should have a urethroscopic and cystoscopic examination to exclude tumor, in either the urethra or the bladder. These examinations do not often discover anything, but occasionally a papilloma is found in the bladder neck or posterior urethra, in association with hemospermia.*

WASHINGTON NEWS

Rise in Health Budget Seen . .
Report on Influenza . .
Death of Simpson . .
Forand Bill . .
Radiation Program . .
Hospital Research . .
PHS-Reorganization Study . .

FEDERAL BUDGET SURPLUS SEEN: HEALTH SPENDING INCREASE ASKED

The Eisenhower administration proposed a federal spending budget of 79.8 billion dollars for the fiscal year starting July 1 and recommended that Congress increase most appropriations for health and medical activities. According to administration estimates, the budget would provide a 4.2-billion-dollar surplus. President Eisenhower asked that this be used to begin paying off the 290-billion-dollar national debt.

The Chief Executive announced before the budget was released that increases would be sought in almost all federal medical and health programs. It was expected that the administration would recommend about 400 million dollars for the medical research activities of the National Institutes of Health, in comparison with the 294 million dollars proposed last year. Congress in 1959 voted 106 million dollars more than the budget request, in a move that the administration opposed.

All told, last year, 3.1 billion dollars was appropriated for the medical and health activities of 20 federal agencies and the government employees' health programs.

In recent years Congress has raised spending for federal medical and health plans over administration requests.

The 4.2-billion-dollar surplus would be the largest since 1948, when the budget was 8.4 billion dollars in the black.

Congress and the economy will have to cooperate with the Eisenhower administration during its final year in office, in order for the surplus to materialize. The lawmakers would have to keep tight reins on spending and approve a requested 600-million-dollar increase in postal rates. And the economy would have to continue prosperous so that revenues would equal the hoped-for 84-billion-dollar intake.

PUBLIC HEALTH SERVICE REPORT ON INFLUENZA

The U. S. Public Health Service reported outbreaks of influenza in nine states.

In all four instances in which laboratory confirmations have been made (Hawaii, Texas, Ohio, and Michigan) the disease was found to be caused by the Asian strain.

Reports had also been received by the National Office of Vital Statistics from Tennessee, Kentucky, California, Nevada, and Utah, but laboratory tests had not been completed in these states.

According to the reports, the disease generally was relatively mild, although in some areas, like Fresno, Calif., large numbers of patients were hospitalized. Schools were closed in Perry County, Tenn., where an "explosive outbreak" was in progress, according to PHS.

PHS said the many scattered outbreaks so early in the influenza season indicated "that the disease was well seeded" in the country and could be expected to appear in many localized concentrations.

PHS has recommended vaccination for certain population groups such as persons aged over 55 who have a chronic disease, persons suffering from heart or pulmonary diseases, and pregnant women.

Persons in these groups who have not been vaccinated should seek their physicians' advice immediately, said PHS.

"In those areas where outbreaks are occurring, the physician may feel it is too late for vaccination, since the disease will probably strike during the several weeks needed for the protective effect of the vaccine to develop," said acting Surgeon General John D. Porterfield. "On the other hand, in communities still free of influenza, the physician may recommend vaccination."

REPRESENTATIVE SIMPSON DIES

Rep. Richard M. Simpson, ranking Republican member of the House Ways and Means Committee, died at Bethesda Naval Hospital. He had been operated on in December for a brain tumor.

A leader of conservative forces in the House and a sponsor of the measure that would encourage physicians and other self-employed persons to plan for their retirement, Representative Simpson was also chairman of the Republican national congressional committee that works to help elect Republican lawmakers.

President Eisenhower declared, "It is with profound regret that I have learned this morning of the passing of Rep. Richard M. Simpson, a veteran and distinguished legislator, who for many years has courageously and conscientiously served his district, the nation, and the Republican party."

Representative Simpson, aged 59, who served in Congress for 22 years, was a major opponent of the controversial Forand bill that would place medical care under the social security program for the first time. He sponsored, along with Rep. Eugene J. Keogh (D., N. Y.), the Keogh-Simpson bill that would provide tax deferrals for self-employed persons who invest money in qualified programs. The measure was overwhelmingly approved by the House last year, and is now before the Senate Finance Committee.

Simpson's death elevated Rep. Noah M. Mason (R., Ill.) to the top Republican spot on the Ways and Means Committee.

(Continued on next page)

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Riseman, J. E. F., *et al.*: Circulation *17*:22, 1958

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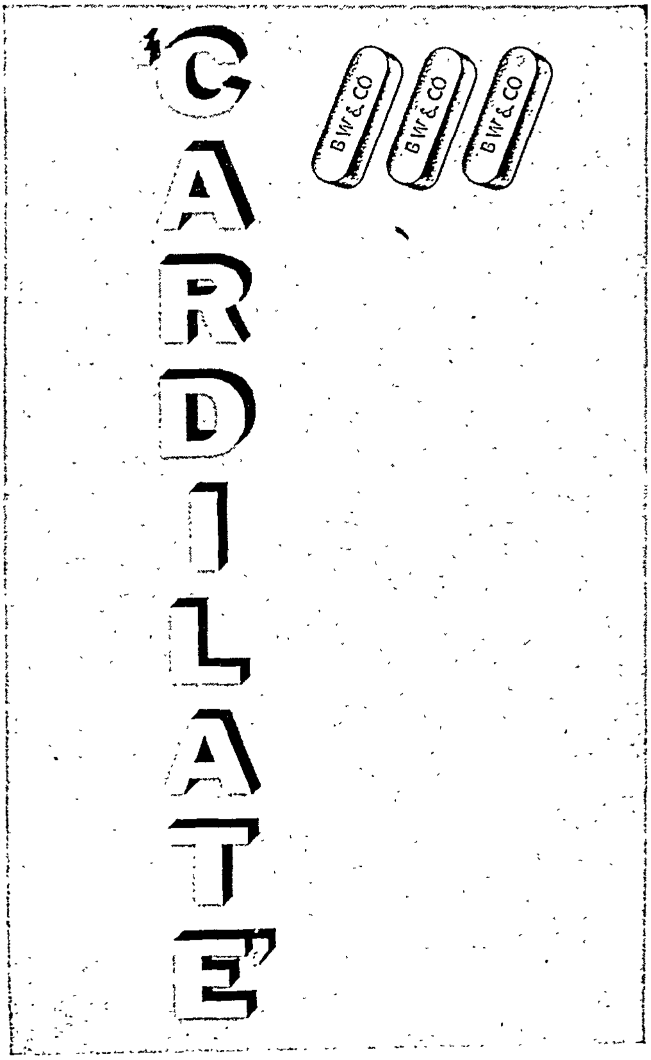


LABOR ASKS PASSAGE OF FORAND BILL

The AFL-CIO began a push for congressional approval of the controversial Forand bill that would interject medical and health care financing into the social security system for the first time.

At a legislative conference of more than 600 key union officials here, AFL-CIO President George Meany declared that "at the very least" Congress should enact higher unemployment compensation benefits "along with the Forand bill to provide medical cost insurance for elderly people who have retired under Social Security."

At the labor conference a pamphlet backing the Forand bill entitled "Can You Afford to Be 65?" was distributed.

However, in a speech before the labor officials, House Majority Leader John McCormack (D., Mass.) did not mention the Forand bill, although he predicted Congress would pass some type of liberalization of the social security program.

Earlier, House Speaker Sam Rayburn (D., Texas) told a news conference that he believed a majority of the House Ways and Means Committee was opposed to the Forand bill. As a result, he said he did not believe "there was a great deal of chance for it" at the current session. However, the House speaker flatly predicted passage of a measure that would liberalize the social security program for totally and permanently disabled persons by removing the present requirement that a person must be at least 50 years of age before becoming eligible for benefits.

CHECKS ON RADIATION STEPPED UP

The Public Health Service announced an intensified program of checking for possibly harmful amounts of radioactivity. As part of the expansion, PHS will issue a monthly report on all radiation information developed.

The report will include data on radiation from all federal and state agencies and private sources and will include "raw data . . . which will be of use to the scientific community."

In other moves to expand the radiation program established to protect the public against any undue concentration of dangerous radioactivity, the Department of Health, Education, and Welfare disclosed the following steps.

—The opening of two new PHS radiation laboratories at Las Vegas, Nev., and Montgomery, Ala. A third laboratory, for special research work on x-ray exposures, is scheduled for completion by late summer in Rockville, Md.

—The planned expansion of the milk sampling network from the present 12 to 60 stations, in order to cover all milk sheds in the country.

—A substantial increase in the numbers of persons from federal, state, and local agencies and industrial concerns being trained for work in radiologic health at the Robert A. Taft Sanitary Engineering Center in Cincinnati.

—A substantial boost in the amount of research at the service's National Institutes of Health and through grants-in-aid. The total for fiscal 1960 is about $5,500,000, compared with about 2 million dollars for last year.

—Completion of plans for the establishment of a radiologic unit in the Food and Drug Administration to conduct research in measurement techniques and methods of decontamination of foods, drugs, and cosmetics.

—Training of more key FDA personnel in instrumentation and radiochemistry, and in use of portable radioactivity measuring equipment, at the Atomic Energy Commission laboratory in New York City.

HOSPITAL RESEARCH EXPANSION

State hospital officers recommended, in a report to the U. S. Public Health Service, that federal spending on research for hospital administration and management be increased from $1,200,000 to 10 million dollars annually.

In addition the administration should ask Congress for funds to survey the need for new hospitals and services in the larger metropolitan areas, "as well as the need for modernization and expansion or possible conversion of existing care facilities," said the state officials after the meeting called by PHS.

The report proposed that PHS, the American Medical Association, the American Hospital Association, and state hospital authorities study and develop guides for the provision of disaster services, where feasible, in the planning of new hospitals.

Another conference of state officials—mental health authorities—recommended that general hospitals be encouraged to admit alcoholics for treatment and that PHS provide courses for state officials on the development of alcoholism program activities.

An investigation of the needs of mentally retarded and borderline adults and the resources available for them was also suggested.

PHS REORGANIZATION STUDY

A possible sweeping reorganization of the U. S. Public Health Service may be forthcoming as the result of a study ordered by PHS Surgeon General Leroy E. Burney.

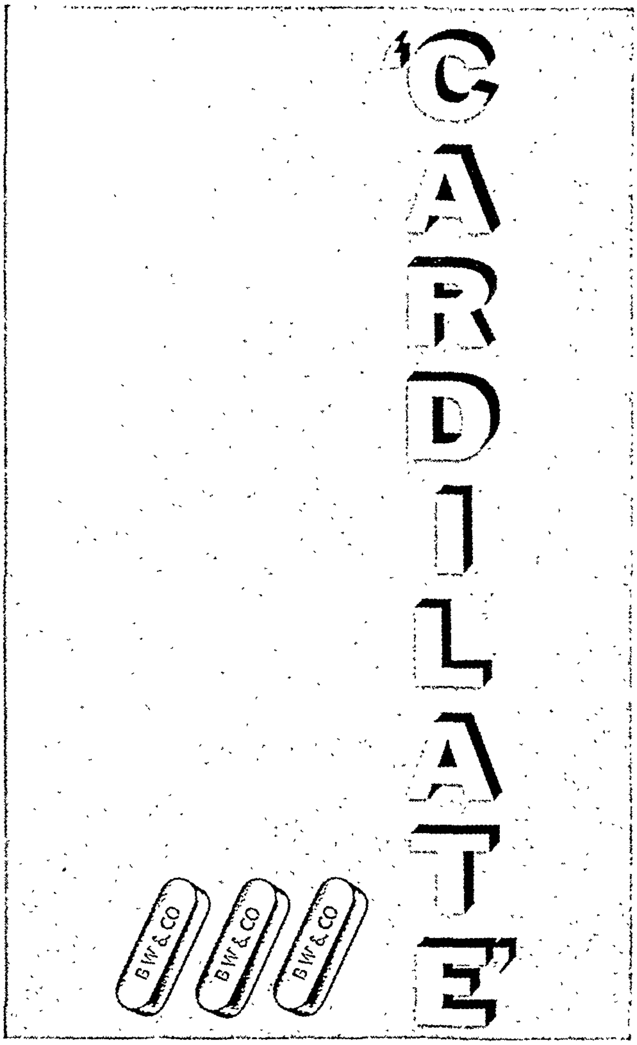
A major purpose of the study is to produce "a clear-cut and balanced statement of the mission of the Public Health Service as it can be seen now for the 1960 decade," said Dr. Burney.

A group of eight PHS officers was furnished with a special staff to help it during the three-month study.

Another goal of the program was to provide "a reasonably detailed outline of the organizational structure of the service, or alternative patterns of organization, which would be most conducive to the effective and efficient accomplishment of that mission."

Last year Congress ordered PHS to develop a long-range program for expanding its environmental health program that covers radiation, air pollution, water pollution, accident prevention, and occupational health. Dr. Burney said that it became obvious later that a review of all of PHS's expanding functions was needed.

Members of the study group are Dr. James Huley (chairman); Margaret Arnstein; Drs. Burnet Davis, Herald Graning, Harold Magnuson, and Donald Galagan; Harry Hanson; and Dr. William Stewart.



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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-Dec. 1.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 25-30.

AMERICAN

1960

January

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 11-13. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, *Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower,* Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, North Carolina Chapter, Hotel Barringer, Charlotte, N. C., Feb. 26-27. For information write Dr. Alexander Webb Jr., 201 Bryan Bldg., Cameron Village, Raleigh, N. C.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-*Treasurer.*

American Academy of General Practice, Philadelphia, Mar. 18-24. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Mo., Executive Director.

American Association for the History of Medicine, Inc., Char S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Insti Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Bro Colorado Springs, Colo., Mar. 21-23. For information write: Dr. Saunders, 40 E. Erie St., Chicago 11.

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American Gastroscopic Society, *Roosevelt Hotel, New Orleans,* M Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Tr

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National Health Council, National Health Forum, Mia Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19 tive Director.

National Multiple Sclerosis Society, New York City, Mar. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Balti Secretary.

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ALLERGIC EMERGENCIES

Roy Patterson, M.D., Ann Arbor, Mich.

Severe constitutional reactions, ranging from dyspnea, cyanosis, and hypotension to collapse and death, sometimes follow apparently slight provocation. Most severe allergic reactions and deaths in recent years have followed the administration of penicillin. To prevent such reactions it is important to refer to the patient's medical history. In the case of penicillin, skin testing is indicated but must be done with caution; cutaneous testing should precede intracutaneous testing, and initial concentrations as low as 0.1 unit per cubic centimeter have been recommended. Reactions that occur in spite of such precautions must be treated promptly by intramuscular injection of 0.3 to 0.5 cc. of 1:1,000 aqueous epinephrine, after which an antihistamine is to be considered. The physician should also have well in mind the steps to take when allergic reactions follow the administration of aspirin to aspirin-sensitive asthmatics.

IMMEDIATE reactions to a foreign material in a hypersensitive person may be of such severity that death results. Such reactions are acute emergencies requiring nmediate therapy and may be termed constituonal reactions, allergic shock, or anaphylactoid hock and are comparable to anaphylactic shock ı animals in many respects. These reactions are ased on an immunological mechanism in either he induced hypersensitive state or the atopic state f spontaneous hypersensitivity. The reaction is resumed to occur as a result of the reaction of the ntibodies of the host to the injected antigen which esults in the release of histamine and possibly other nediators. The hypersensitive state may be demontrable in many cases by positive results of skin ests to the offending antigen, although in some ases of severe penicillin sensitivity there is no ositive reaction.[1]

Types of Reactions

Immediate, severe reactions may result from reatment with penicillin, foreign serum used as ntitoxin, hyposensitization treatments with allergenic materials, insect stings in sensitized persons, and rupture of a hydatid cyst.[1A] Most severe allergic reactions and deaths in recent years have occurred from the administration of penicillin. Other injected materials, such as ACTH and penicillinase, have been reported to cause immediate reactions, presumably on the basis of a hypersensitivity reaction to a foreign protein, but it is always difficult to

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From the Department of Internal Medicine, University of Michigan Medical School.

Read in the Session on Allergy before the Section on Miscellaneous Topics at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 11, 1959.

derive certainty from some of these reports that the reaction has not occurred from a syringe contaminated with penicillin and used in a penicillin-sensitive patient.

The symptoms of the severe constitutional reaction may vary. Dyspnea, cyanosis, fall in blood pressure, unconsciousness, collapse, coma, and death all may occur in the individual case, but all of these symptoms need not be present.[2] The reaction may be immediate, occurring at the instant of the injection, but usually it occurs within 30 minutes. Death may occur immediately or in minutes to hours after the onset of the reaction.

Precautions for avoiding the severe allergic reaction depend on the avoidance of administration of materials likely to cause a reaction where there is evidence that it may occur. The patient's medical history is of great importance in determining the risk of administration of penicillin and horse serum, and it is necessary to ask every patient given these substances specifically about a history of sensitivity to penicillin or allergic symptoms after exposure to horses or horse serum. Obvious as this would appear to be, fatalities nevertheless have occurred in patients with a known penicillin allergy who were not asked about the possibility of previous reactions prior to the administration of this drug.[3] The patient cannot be relied on to volunteer this information. In a case of known drug allergy, this information must be displayed prominently on the patient's record. Neglect of this detail has resulted in deaths in hospitals from administration of penicillin in instances where the history was obtained by one physician and penicillin administered by another. Oral administration of penicillin probably is safer than intramuscular injection, but this is no insurance against a fatal reaction since severe penicillin reactions have occurred after oral administration of penicillin and even after use of penicillin lozenges.[4]

Skin testing is indicated in the case of an uncertain history of penicillin sensitivity when penicillin seems the antibiotic of choice. A positive result of a skin test suggests that an immediate, severe reaction is likely. A negative result of a skin test to penicillin suggests that an immediate reaction is less likely to occur, but the severe reaction is not excluded by a negative skin test result. Skin tests for penicillin sensitivity must be done with caution, since severe reactions to penicillin skin tests have occurred. Intracutaneous testing should be preceded by cutaneous testing. Published recommendations for initial concentrations of penicillin to be used in testing have varied from 0.1 to 300,000 units per cubic centimeter, and, in a patient suspected of penicillin sensitivity, the cutaneous tests should be initiated at very dilute concentrations. The testing then may be continued by serial 10-fold increases in concentration and subsequently by intracutaneous testing with 10 to 10,000 units per cubic centimeter. The incidence of these reactions appears to be increased in patients with a histor of atopic disease, so that additional caution i warranted in this group. Any material which ha the potentiality of causing an allergic reactio should be injected in an extremity in an area wher there is sufficient room to apply a tourniquet abov the injection site if a reaction should occur.

The prevention of fatal reactions to bee, wasp or yellow jacket stings can be based on avoidanc of the insect, immunization to these insects, an emergency treatment by the patient himself.

Some advice can be given to patients who ar hypersensitive to bee venom regarding measure that can be taken to avoid and alleviate bee sting This advice is based on observations by Adria Wenner, who has been studying bee behavior the University of Michigan.[5] Brown, black, or re clothes with a worsted or flannel texture, brig objects such as bright jewelry, and the odor perspiration appear to cause bees to sting mor readily. Swatting or swinging at bees will increas the likelihood of being stung, and a standing pe son is more likely to be stung than a person who sitting or lying down. Consequently, if a person approached by a few bees, sitting or lying quietl is advisable, and attacking bees may be discourage by crawling through bushes or under large object The explanation for some of these observations ma be that any appearance or activity of a huma which simulates that of a bear may stimulate a b to sting, since the bear is a natural enemy of t bee. After being stung, the victim immediate should attempt to remove the stinger by scrapin with the fingernail, since contraction of the stingi apparatus continually injects venom into the tissu Grasping of the stinger will only force more veno into the wound. Since there is no certain metho of avoiding insect stings, immunization of t hypersensitive person should be carried out wi use of an extract of the insect producing the rea tion, and appropriate drugs should be carried wi the patient at all times of possible exposure f immediate use after the sting. While sublingual a ministration of isoproterenol (Isuprel) hydrochlori and oral administration of antihistamines have bee suggested by some physicians, others feel that th danger is such that the patient should be instructe in the use of injectable epinephrine which is the administered by the patient while a physician called.

Skin or ophthalmic testing is imperative prior t the use of foreign serum used as antitoxin. If positive reaction occurs, the substitution of an ant toxin from a different species such as bovine ant toxin is necessary and must be tested again pri to use. Where there is no available substitute, de sensitization may be carried out in the sensiti patient with extreme caution. Encouraging the use of adequate "booster" doses of tetanus toxoid in the general population, particularly horse-sensitive and horse serum-sensitive persons and those exposed to trauma in dirty localities will, of course, reduce the necessity of the use of tetanus antitoxin and thereby the reaction incidence.

Treatment

When an immediate reaction has occurred, treatment must be initiated promptly, since even short delays may be fatal. Therefore, the materials necessary for treatment should be kept readily available in a definite place in the physician's office. If the injection of the drug causing the reaction has been given in the arm, a tourniquet is placed above the site of injection to slow down absorption. Epinephrine is given in the opposite arm, with use of 0.3 to 0.5 cc. of 1:1,000 aqueous epinephrine. The intramuscular route is best, because, if the patient is in shock, the subcutaneous route of injection may result in very slow absorption. After the epinephrine has been injected intramuscularly, massage of the site of injection will increase the rapidity of absorption. To further delay absorption of the antigen, an additional 0.3 cc. of 1:1,000 aqueous epinephrine is given also in the site of the previous antigen injection.

An intravenously given antihistamine is the next measure to be considered, with use, for example, of 50 to 80 mg. of diphenhydramine (Benadryl) hydrochloride injected slowly intravenously in an adult. Administration of oxygen should be started immediately if it is available. After the above measures have been instituted, the patient may have recovered sufficiently to make further treatment unnecessary. However, further intensive treatment may be necessary. Administration of epinephrine may be repeated every 15 to 20 minutes. For persistent hypotension, an intravenous drip infusion of 5% dextrose in water should be started, and therapy with a vasopressor agent such as levarterenol should be commenced at a rate sufficient to maintain the blood pressure at reasonably normal levels.

If bronchospasm is an important feature of the problem, as demonstrated by audible wheezing or by examination of the chest, aminophylline can be administered intravenously in a dose of 0.25 Gm. in 10 cc. of sterile saline solution over a 10-minute period. It is always wise to keep in mind that deaths have occurred from too rapid intravenous administration of aminophylline. If there is no evidence of bronchospasm and if the patient is in shock, intravenous administration of aminophylline may promote a further fall in blood pressure and would, therefore, be contraindicated. Laryngeal edema or laryngospasm may necessitate a tracheotomy during the course of the reaction.

These measures cover the primary treatment of the anaphylactic type of reaction. If the patient does not respond rapidly, and if all of the above measures have been carried out, the intravenous administration of adrenal corticoid steroids such as hydrocortisone sodium succinate in a dose of 100 mg. is indicated. Adrenal corticoid steroids are not the first choice of treatment, since they are relatively impotent antianaphylactic agents and also are too slow in action to be lifesaving in a few minutes, but in a case in which the other measures have not resulted in complete control of the reaction intravenously given steroids are indicated for whatever additional benefit they may offer.

The reaction due to aspirin in the aspirin-sensitive asthmatic is a problem requiring particular attention. The reaction generally occurs about 20 minutes after the ingestion of aspirin and the symptom is bronchial asthma of extreme severity. Death may occur shortly after onset of the asthmatic attack or the patient may spontaneously recover. Emergency treatment consists of 0.3 to 0.5 cc. of 1:1,000 aqueous epinephrine given intramuscularly and removal of the aspirin by a stomach tube. These patients never should be given aspirin to see if it will cause a reaction, and they should be warned of the sources of aspirin in "cold" remedies and advised to take no medicament unless they know it does not contain aspirin.

Since the allergic reaction may be dramatic and rapid therapy imperative, it is best for the physician to review the steps he will take in preparation for such an occurrence. The calmness of the physician in the face of impending catastrophe is probably one of the most important contributions to the management of allergic emergencies.

Summary

The problem of the immediate, severe allergic reaction to penicillin, foreign serum used as antitoxin, hyposensitization treatment with allergenic materials, insect stings in sensitized persons, and ingestion of aspirin must be dealt with by all possible measures for avoidance and rapid therapy with known remedies for these reactions to prevent a fatal result.

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CLINICAL USE OF DEXAMETHASONE

ROLE IN TREATMENT OF PATIENTS WITH ARTHRITIS

Joseph L. Hollander, M.D., Philadelphia

The results of experience with cortisone and six other corticosteroids in patients with rheumatoid arthritis have been tabulated for comparison. The seven hormones all have potent ameliorating effects in that they permit increased function without greatly affecting the course of the disease. Some of the disagreeable systemic side-effects can be avoided by injecting the hormone into the inflamed joints, and few serious complications have been observed in more than 92,000 such injections in 3,000 patients. When side-effects occur, the hormone can be withdrawn provided this is done gradually over periods of at least several months. In 72 patients treated with dexamethasone increased appetite, weight gain, and mental stimulation were frequently encountered as side-effects. It is still not the ideal corticosteroid, but it is a useful addition to the list.

Research chemists in the United States have shown great resourcefulness in the synthesis and production of cortisone and in changing the cortisone formula in a variety of ways in an effort to make the steroid more useful, with increased potency and fewer undesirable side-effects. Some of these changes are illustrated in the figure. Early in the synthesis of this drug it was found that the substitution of a hydroxyl group at C-11 for the oxygen was an improvement. This made compound F, hydrocortisone, the 1951 model, largely supersede the 1949 model, compound E, cortisone. Clinicians [1] soon found that, to paraphrase an old song, "Anything E could do, F could do better," and particularly that therapy with hydrocortisone was tremendously more palliative when the drug was used in treatment by injection into arthritic joints.[2] Hydrocortisone is still, in my opinion, the best steroid for treating rheumatoid arthritis in children.

In 1954 it was found that the potency of the steroid was greatly increased by addition of fluorine in the 9-alpha position.[3] This fluorohydrocortisone had some advantage in topical therapy for skin conditions and for control of adrenal cortical hypofunction (Addison's disease), but it had such a tremendous salt-retaining effect that it had few therapeutic uses and none for rheumatoid arthritis either systemically [4] or locally.[5]

In another brilliant advance, an unsaturated double bond was induced between the first two carbon atoms of the steroid; the delta-1 derivative of cortisone was called prednisone and the similar derivative of hydrocortisone was called prednisolone, both possessing greater antirheumatic potency and less of a sodium-retaining effect than the original corticosteroids.[6] These 1955 models almost completely superseded the earlier types in the treatment of rheumatoid arthritis, but it was found that they were still not the final answer to the problem of side-effects since they produced even more peptic ulcers and osteoporosis, although much less edema. They are still among the best cortisone drugs for treating rheumatoid arthritis.

In 1957 two new competing models were offered. Whereas both had slightly greater potency than prednisone or prednisolone, they had vastly different properties. Methylprednisolone had a methyl group attached to the sixth carbon atom, which may have slightly reduced some of the side-effects but not nearly to the extent stated in the adverti ing, which claims that this is the steroid that "hi the disease but spares the patient."[7]

In my experience with 47 patients with rheum toid arthritis, methylprednisolone has been foun to have practically no advantage over prednisolon except that there may be a somewhat decrease tendency to menstrual irregularity and purpura i female patients taking this steroid. Other sid effects seem about the same as from the "predn steroids."

The other 1957-model steroid has proved e tremely interesting. With the addition of bot fluorine at the 9-alpha position and a hydrox group at the 16, the salt-retaining property fluorohydrocortisone was completely neutralize to the extent that no sodium retention occurre with its use. Mental stimulation was also elim nated, and appetite decreased when this poter antirheumatic steroid, triamcinolone, was use Some new side-effects were noted, including co stipation, a peculiar weakness not caused by pota sium loss, and a great deal of flushing, dryness, an loss of elasticity of the skin. Freyberg and co-wor ers [8] had pointed out these effects, and this seemin affinity for the skin suggested the studies on sk disease, in the treatment of which triamcinolone i most useful. My studies (with others) [9] in 33 patient with both psoriasis and arthritis have shown triam

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Read before the Section on General Practice at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

cinolone, administered orally, to be the most effective steroid for control of both the psoriatic skin lesions and the joint symptoms and signs in most such cases. It is also useful in the treatment of patients with cardiac decompensation who need steroid therapy for rheumatoid arthritis, since it does not produce any edema. Triamcinolone as the acetonide is now used for topical application in patients with skin conditions.[10]

Last year another "new model" antirheumatic steroid was introduced by the clinical work of Boland and Headley [11] and Bunim and co-workers.[12] Dexamethasone, introduced 10 years after work on cortisone was started, differs from triamcinolone only in that a methyl group replaces the OH at C-16. The wonder of chemistry is how this relatively minor change could make so much difference in its effects. With a daily dose of 3 mg. or less, the arthritis-controlling effect of 12 mg. per day of triamcinolone or methylprednisolone, 15 mg. per day of prednisolone, or 60 mg. per day of hydrocortisone, the natural steroid of the adrenal gland, can be duplicated. This is the most potent corticosteroid, milligram for milligram, now available. However, potency alone means little unless there is also a reduction of side-effects.

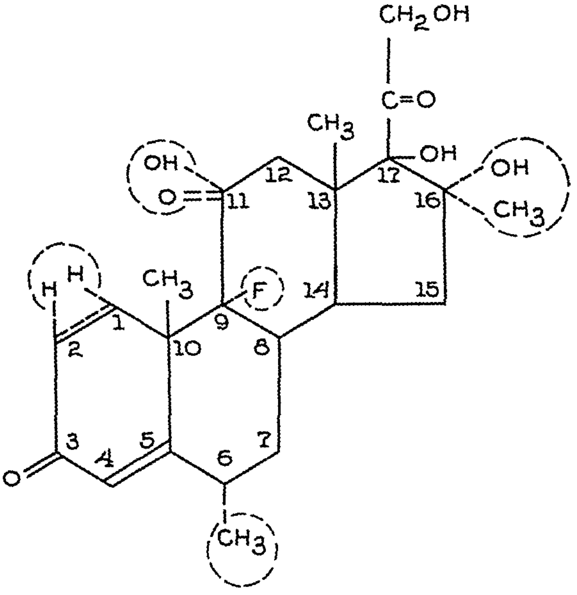
Whereas triamcinolone suppresses appetite and has no mentally stimulating or euphorigenic effect, the minor change in formula to dexamethasone has reversed this, and this steroid produces the greatest stimulation of appetite and mental processes of all the cortisone family. In 72 rheumatoid arthritic patients treated with this new steroid, nearly 70% have shown these effects in some degree. This is certainly an advantage in the management of underweight, anorexic, and depressed rheumatoid arthritic patients. It is not an unmixed blessing, however, since treatment with this hormone has brought more trouble in patients already overweight or jittery. Patients treated with this steroid must be carefully chosen.

The weakness often seen in patients receiving triamcinolone is not seen with dexamethasone, nor is the dryness of the skin, flushing, or loss of elasticity of the skin noted with use of this steroid—but the antipsoriatic effect seen with use of triamcinolone is also lost. Thus, dexamethasone has little value in treating patients with psoriasis complicating arthritis.

Dexamethasone apparently has less of a tendency to produce or aggravate diabetes and may prove to be the preferred steroid for treatment of arthritic patients who have even a mild diabetic tendency. In my experience there also has seemed to be somewhat less of a tendency to gastric irritation than with prednisone or triamcinolone.

The moral of the story so far is this: Dexamethasone is another useful addition to the cortisone family but still is not the final answer. We seem now to be in an era of "special-purpose steroids." The "new models" all have their own set of effects which make them preferable for special cases but not necessarily better than hydrocortisone or prednisolone as a "general-purpose steroid" for treatment of patients with rheumatoid arthritis.

In the table are summarized the comparative antirheumatic doses and side-effects of these corticosteroids currently available for treatment of arthritis. Even a cursory perusal will show the differences, advantages, and disadvantages of each, but it should be pointed out here that all still have most of the unwanted effects in some degree. The table shows mainly that a steroid preparation can now be chosen which will best fit the needs of a particular patient. This is somewhat analogous to the choice of one of the digitalis glucosides, one of the sulfonamides, or one of the antibiotics for an individual treatment problem. Since all these hormones can produce similarly unwanted side-effects, we will discuss them together as "the cortisone group." It should be noted that it makes little difference in the risk whether the hormone is used alone or in combination with other agents such as aspirin, buffers, or tranquilizers.



Corticosteroid structural formula with ringed radicals to show substitutions for production of newer steroids. Cortisone: 11 oxygen, no double bond at 1,2, no ringed additions. Hydrocortisone: 11 hydroxy, otherwise same as cortisone. Fluorohydrocortisone: addition of fluorine at 9 to hydrocortisone. Prednisone: cortisone with double bond between 1,2. Prednisolone: hydrocortisone with double bond between 1,2. *Methylprednisolone: methyl group at 6* to prednisolone. Triamcinolone: fluorine added at 9, hydroxyl at 16 to prednisolone. Dexamethasone: fluorine added at 9, methyl at 16 to prednisolone.

Side-effects and Precautions

Among the undesirable side-effects from the cortisone drugs is the so-called moon face, of which all physicians have become aware, a part of the clinical picture of adrenal cortical hyperfunction (Cushing's syndrome). This is apparently produced by redistribution or excessive deposition of fat in the subcutaneous tissue of the face and neck. Often found with this are such other features of this syndrome as hypertension, obesity, sodium retention with edema, development of striae on the skin, and still other relatively minor nuisances such as acne or hirsutism.

Much more serious, however, is the tendency of the cortisone drugs to produce osteoporosis of the skeleton through their catabolic or nitrogen-losing effect. This is produced by long-term administration, particularly if large doses have been given. The postmenopausal state in women, advanced middle age in men, and rheumatoid arthritis itself all tend to produce osteoporosis, so there is definite danger of compression fractures of vertebrae or pathological fractures of long bones when large doses of the corticosteroids are administered to such patients over prolonged periods. The concomitant use of anabolic hormones such as testosterone, estrone, or newer synthetic anabolic hormones may diminish this danger but do not eliminate it.

Treatment with cortisone and its related compounds is by no means a cure for rheumatoid arthritis. Their use does not stop the progress of this inflammatory disease. In addition, it has been shown that these hormones do not affect the cause of the condition but only suppress the manifestations of the disease to some degree.

At this point one might readily agree with those who ask, "Why use cortisone at all, since it may do more harm than good?" In answer, I can quote from my experience with over 1,000 patients that there are 20 patients better off for having been treated with the hormones for every one made worse in some manner from receiving such therapy. This does not mean that 20 patients are much improved for every one worse but that the calculated risk of marked *side-effects* or of *ineffectiveness* is about 5%.

Advantages.—What, then, can be expected from the cortisones, on the positive side of the ledger? Here is where the conservative physicians are separated from the therapeutic enthusiasts, and here the philosophy of cortisone therapy must be considered.

Comparative Effects of Corticosteroids

	Cortisone	Hydrocortisone	Prednisone	Prednisolone	Methylprednisolone	Triamcinolone	Dexamethasone
Equivalent daily dose, mg.	75	60	15	15	12	12	3
Edema, sodium retention ..	++++	+++	+	++	+	0	+
Weakness or potassium depletion	+++	++	+	+	+	++	+
Hypertension	++	+	+	++	+	+	+
Mental stimulation	+++	+	++	++	+	0 to —	++++
Increased appetite and weight gain	++	++	++	++	+	—	++++
Peptic ulcer	++	+	+++	+++	++	+++	++
Purpura	+	+	+++	+++	++	+++	++
Moon face	+++	++	++	++	++	+++	++
Hirsutism	++	++	++	++	++	++++	+
Skin effects	+	+	+	+	+	++++	+
Osteoporosis	+++	++	+++	+++	+++	+++	++
Diabetes	++	++	+++	++++	+++	++	+
Infections	++	++	++	++	++	++	++
Topical effect	+	+++	+	+++	++	+++	++
Adrenal atrophy	+++	+++	+++	+++	+++	+++	+++

Because of the depressing action of corticosteroids on fibroblastic activity and on the immune mechanism of the body, a diminished resistance to infection usually results from their use. The anti-inflammatory action of cortisone also tends to mask the usual signs of infection, making it difficult to trace down or treat promptly. From these same effects, use of the steroids may lead to perforation or hemorrhage of a peptic ulcer or rupture of an inflamed diverticulum. If the patient has a diabetic tendency, cortisone administration will bring out overt diabetes, and a patient with a psychotic tendency may likewise be precipitated into frank psychosis. Latent tuberculosis may flare up in a patient taking cortisone. All these risks must be considered before starting any patient on therapy with cortisone or its derivatives, remembering that dexamethasone and other newer steroids only change the proportionate risk of some of the effects but do not eliminate them.

The closest analogy that can be drawn is with digitalis treatment for cardiac decompensation. Digitalis, also a steroid, does not cure heart disease, does not stop the progress of the pathological changes, and also does not affect the cause of the condition. The actual effect of digitalis on the patient with heart disease is an amelioration of symptoms by improvement of cardiac function, and likewise the action of cortisone on patients with rheumatoid arthritis is amelioration of symptoms and improvement of musculoskeletal function.

Many arthritic patients are working daily, in spite of their rheumatoid arthritis, who before taking cortisone could hardly care for their most fundamental needs at home. They still have arthritis, but the pain is controlled or made bearable, and their muscle power, nutrition, and ability to work have been greatly increased. They can live more normally in spite of their chronic disease. Is this not analogous to the cardiac patients who could not climb stairs or even walk about, with dyspnea, precordial pain, and edema of the extremities, who, after digitalization, can perform their regular jobs?

Once the cardiac patient has been digitalized for decompensation, use of the drug is expected to continue indefinitely, and so we should view the use of cortisone for patients with rheumatoid arthritis severe enough to justify "cortisonization." Remembering that cardiac patients may still die in spite of digitalization, or may have toxic effects from the drug during its administration, we must not be unduly surprised that arthritic patients sometimes become worse in spite of cortisone therapy or develop side-effects of a dangerous character.

What this analogy helps to point up also is that the patient must have rheumatoid arthritis acutely or severely enough to be "arthritically decompensated" before the decision to "cortisonize" him is justified. The mere presence of stiffness, pain, and swelling of joints does not constitute sufficient indication for cortisone therapy, but if these same symptoms and signs are of such a degree as to prevent the patient from carrying out his normal functions, or even enjoying life at all, in spite of adequate amounts of aspirin, rest, physical therapy, or perhaps chloroquine or gold salt therapy, I believe the time has arrived to make the fateful decision to start treatment with cortisone. Here the risks of cortisone therapy must be weighed against the increasing debility, and the 1-in-20 chance of harm is justified by the 20-to-1 chance of improvement in symptoms and function. The patient, or a responsible relative, should be made aware of the risk but not in such a way as to alarm him unduly.

Long-term Steroid Therapy

Having once made the decision to give the arthritic patient therapy with cortisone, the physician must face the fact that he is dealing with a chronic, often lifelong, disease and cannot expect to withdraw the steroid easily without prompt and often severe relapse. When used for chronic disease, cortisone and its "relatives" can only be withdrawn gradually and by small decrements over periods of at least several months.

As said before, for each patient with serious complication from the use of cortisone, there are 20 who are better off because of therapy with the hormone, albeit with some of the minor side-effects. It is obvious why we are so conscious of these serious effects—we only see at frequent intervals those patients who are having trouble. It is the old parable of the lost sheep—we don't worry about the "ninety and nine" safe in the fold, but the lost one takes all of our concern.

The physician starts by giving the patient moderate doses of the steroid best suited to his needs, enough only to improve the function and make symptoms more bearable. He should not try to give "loading doses" as originally advised in the earlier literature nor try to suppress symptoms completely. The optimum dose of the corticosteroids is the minimum amount which will make the disease bearable. He rarely gives more than 75 mg. per day of cortisone and 60 mg. per day of hydrocortisone, no more than 15 mg. per day of prednisone or prednisolone, 12 mg. of triamcinolone or methylprednisolone, or 3 mg. of dexamethasone, gradually decreasing the dose, if possible. Aspirin is given along with the steroid and the patient treated generally as well. In case of side-effects or even infection, surgical emergency, or emotional crisis, he should not do what has been so disastrously done in the past, i. e., stop administration of the steroid in panic. He should increase the dosage, in addition to giving all necessary measures, and taper it down again after the emergency is over. If reasonable doses of steroids produce little benefit in the arthritic patient yet do produce side-effects, he should gradually discontinue administration of the hormone over a period of several months—never stop it precipitately, or an acute adrenal insufficiency will result. Cortisone is the medicinal crutch of the arthritic patient, and it should not be snatched away or the patient will fall.

Intrasynovial Steroid Therapy

In many cases of rheumatoid arthritis, and in most cases of severe osteoarthritis, bursitis, and other forms of rheumatism, the severe discomfort or threatened crippling is apparent in only one or a few joints. When this is so, it is far more effective and less dangerous not to "soak the whole machine in oil" by giving steroids systemically but to "put a drop of oil where it squeaks" and simply inject a little of the hormone into the inflamed joint or joints. With use of repeated injections every few weeks on an "as needed" basis, in this way, the dangers of systemic hormone therapy can be obviated.[2] Over 3,000 patients with more than 92,000 injections have been so treated in the past eight years.[13] Aside from 14 infections produced by the technique I have seen few other serious effects. I have yet to see any joint develop ankylotic deformity in a patient under such therapy, but almost 1% of patients develop some instability in long-treated joints. The aseptic technique for injection must be carefully done, although simple. The technique for injecting the joints must be studied carefully, and skill must be acquired by practice so that the joint space can be quickly and painlessly entered.

Follow-up studies [13] have been done on many of these patients over the past eight years and the injections have been found to remain helpful in giving weeks of relief from joint pain. In addition, bursae and inflamed tendon sheaths have been injected [14] with various esters of hydrocortisone and prednisolone, with symptomatic relief. In 1955 it was found that prednisolone tertiary-butylacetate had a longer effect than the older and simpler esters of either hydrocortisone or prednisolone.[13a] More recently, esters of triamcinolone, methylprednisolone, and dexamethasone have been tried but none by redistribution or excessive deposition of fat in the subcutaneous tissue of the face and neck. Often found with this are such other features of this syndrome as hypertension, obesity, sodium retention with edema, development of striae on the skin, and still other relatively minor nuisances such as acne or hirsutism.

Much more serious, however, is the tendency of the cortisone drugs to produce osteoporosis of the skeleton through their catabolic or nitrogen-losing effect. This is produced by long-term administration, particularly if large doses have been given. The postmenopausal state in women, advanced middle age in men, and rheumatoid arthritis itself all tend to produce osteoporosis, so there is definite danger of compression fractures of vertebrae or pathological fractures of long bones when large doses of the corticosteroids are administered to such patients over prolonged periods. The concomitant use of anabolic hormones such as testosterone, estrone, or newer synthetic anabolic hormones may diminish this danger but do not eliminate it.

Treatment with cortisone and its related compounds is by no means a cure for rheumatoid arthritis. Their use does not stop the progress of this inflammatory disease. In addition, it has been shown that these hormones do not affect the cause of the condition but only suppress the manifestations of the disease to some degree.

At this point one might readily agree with those who ask, "Why use cortisone at all, since it may do more harm than good?" In answer, I can quote from my experience with over 1,000 patients that there are 20 patients better off for having been treated with the hormones for every one made worse in some manner from receiving such therapy. This does not mean that 20 patients are much improved for every one worse but that the calculated risk of marked side-effects or of ineffectiveness is about 5%.

Advantages.—What, then, can be expected from the cortisones, on the positive side of the ledger? Here is where the conservative physicians are separated from the therapeutic enthusiasts, and here the philosophy of cortisone therapy must be considered.

Comparative Effects of Corticosteroids

	Cortisone	Hydrocortisone	Prednisone	Prednisolone	Methylprednisolone	Triamcinolone	Dexamethasone
Equivalent daily dose, mg.	75	60	15	15	12	12	3
Edema, sodium retention ..	++++	+++	+	++	+	0	+
Weakness or potassium depletion	+++	++	+	+	+	++	+
Hypertension	++	+	+	++	+	+	+
Mental stimulation	+++	+	++	++	+	0 to —	++++
Increased appetite and weight gain	++	++	++	++	+	—	++++
Peptic ulcer	++	+	+++	+++	++	+++	++
Purpura	+	+	+++	+++	++	+++	++
Moon face	+++	++	++	++	++	+++	++
Hirsutism	++	++	++	++	++	++++	+
Skin effects	+	+	+	+	+	++++	+
Osteoporosis	+++	++	+++	+++	+++	+++	++
Diabetes	++	++	+++	++++	+++	++	+
Infections	++	++	++	++	++	++	++
Topical effect	+	+++	+	+++	++	+++	++
Adrenal atrophy	+++	+++	+++	+++	+++	+++	+++

Because of the depressing action of corticosteroids on fibroblastic activity and on the immune mechanism of the body, a diminished resistance to infection usually results from their use. The anti-inflammatory action of cortisone also tends to mask the usual signs of infection, making it difficult to trace down or treat promptly. From these same effects, use of the steroids may lead to perforation or hemorrhage of a peptic ulcer or rupture of an inflamed diverticulum. If the patient has a diabetic tendency, cortisone administration will bring out overt diabetes, and a patient with a psychotic tendency may likewise be precipitated into frank psychosis. Latent tuberculosis may flare up in a patient taking cortisone. All these risks must be considered before starting any patient on therapy with cortisone or its derivatives, remembering that dexamethasone and other newer steroids only change the proportionate risk of some of the effects but do not eliminate them.

The closest analogy that can be drawn is with digitalis treatment for cardiac decompensation. Digitalis, also a steroid, does not cure heart disease, does not stop the progress of the pathological changes, and also does not affect the cause of the condition. The actual effect of digitalis on the patient with heart disease is an amelioration of symptoms by improvement of cardiac function, and likewise the action of cortisone on patients with rheumatoid arthritis is amelioration of symptoms and improvement of musculoskeletal function.

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Summary and Conclusions

Administration of dexamethasone, like that of other cortisone derivatives, produces a potent ameliorating effect on patients with the symptoms of rheumatoid arthritis, which permits increased function, without greatly affecting the progress of the disease. The cortisone drugs may be termed the medicinal crutches of the arthritic patient. Dexamethasone, like the other cortisone drugs, produces frequent and sometimes troublesome side-effects. Increased appetite, with weight gain, and mental stimulation were frequently encountered in 50 of 72 patients so treated. Patients with rheumatoid arthritis should not be started on therapy with cortisone or its newer derivatives unless the disease is markedly active and more conservative treatment measures have proved inadequate. All the "cortisone family" of steroids can produce similar side-effects, but relative differences in side-effects produced by each make it possible to select a steroid best suited to the therapeutic needs of the individual patient.

Intra-articular therapy with hydrocortisone or its derivatives may suffice for local palliation of arthritis in a patient in whom only one joint or a few joints are severely disabled, thus avoiding the hazards of systemic steroid use. Dexamethasone is a useful and welcome addition to the family of "special-purpose steroids," but it is still not the ideal steroid for the treatment of patients with rheumatoid arthritis.

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DIFFERENTIAL DIAGNOSIS OF THE NEPHROTIC SYNDROME.—Examination of the serum proteins in patients with a clinical picture of the nephrotic syndrome may be helpful in differentiating nephrosis due to glomerulonephritis from systemic lupus erythematosus and other diseases associated with renal involvement, when other characteristic changes are lacking. Patients with the nephrotic syndrome resulting from glomerulonephritis showed a greatly increased alpha-2 fraction and reduced gamma globulin, in contrast to the relatively normal alpha-2 fraction and normal gamma globulin observed in patients with the nephrotic syndrome due to systemic lupus erythematosus and other diseases with renal manifestations.—M. A. Ogryzlo, M.D., M. Maclachlan, M.D., J. A. Dauphinee, M.D., and A. A. Fletcher, M.D., The Serum Proteins in Health and Disease, *The American Journal of Medicine*, October, 1959.

USE OF DEXAMETHASONE IN EYE DISEASE

Dan M. Gordon, M.D., New York

Dexamethasone is the newest corticosteroid preparation to be introduced in ophthalmology. The indications for the use of dexamethasone in ophthalmology are similar to those for the other corticosteroid preparations. Therapy with dexamethasone is symptomatic therapy, and the indications for its use in ophthalmology are inflammation, allergy, edema, granulation tissue, and certain infections. More specifically, the common diseases for which dexamethasone therapy is indicated are as follows: orbital pseudotumor, exophthalmos, blepharitis, acute inflammation of meibomian glands, conjunctivitis, retention granuloma, episcleritis, scleritis, keratitis, corneal ulcer, ocular allergies, herpes zoster, uveitis (iritis, iridocyclitis, and choroiditis), sympathetic ophthalmia, optic and retrobulbar neuritis, certain retinopathies, perivasculitis, temporal arteritis, and postoperative reactions. In the presence of infection, concomitant use of an antimicrobial is mandatory. The local contraindications to use of dexamethasone in ophthalmology are keratitis due to the virus of herpes simplex and certain exanthemas, as well as keratitis due to fungi. The exanthemas which are known to be adversely influenced by topically given corticosteroids are chickenpox and smallpox.

I have successfully treated two patients with keratitis due to rubella with corticosteroids, one of them with topically given dexamethasone. The adenovirus ocular infection familiarly known as APC disease or adenopharyngeal conjunctival inflammation is beneficially affected by topical therapy with dexamethasone. There is considerable confusion in the literature on this, as many authors and ophthalmologists mistakenly believe that, because most cases of herpes simplex keratitis are adversely affected by topically given steroid preparations, all virus keratitides and conjunctivitides are adversely affected by dexamethasone and the other topically applied steroids. This is not true, as the topically given steroids, including dexamethasone, have been demonstrated to be beneficial in many of the virus oculopathies, including herpes zoster and adenovirus inflammations of the conjunctiva and cornea as well as in many cases of so-called epidemic keratoconjunctivitides.

The physician should be especially wary of treating any patients with a present or impending herpes simplex (dendritic) keratitis. When herpes simplex involves the cornea, it characteristically causes a dendritic or branching lesion or lesions in the superficial layers of the cornea. At the terminus of each line or branch there is a knob. The involved cornea tends to become anesthetic to the touch. The branching or dendritic lesions stain with fluorescein. The practitioner also should be especially concerned when the condition of any patient who is on topical steroid therapy worsens or does not improve appreciably after one or two days. Such a patient should be reexamined with a view to ascertaining whether he has dendritic keratitis. In those areas in which fungi tend to be endemic, one should always be on the alert for fungal keratitis. Patients with this infection are not helped by topical administration of antimicrobials or steroids either.

It is important to bear in mind that the success of topically administered dexamethasone or the other steroids depends, in indicated cases, on the frequency of administration and on the selection of the proper route of administration. When the ocular disease under treatment can be seen with the naked eye, that is, when the lids, conjunctiva, cornea, and, possibly, the iris, are involved, frequent applications of dexamethasone may reach the site of the lesion and be successful clinically. However, when the condition under treatment cannot be seen with the naked eye—that is, when it lies behind the iris—systemic routes are mandatory. It is the failure to observe this indicated route as well as the failure to use doses sufficiently large or frequent which is so commonly responsible for most steroid failures. In general practice steroids have proved valuable in the treatment of the superficial lid and external eye diseases, such as blepharitis and conjunctivitis. In ophthalmology the steroids have revolutionized the therapy of many of the intraocular inflammations, especially iritis, iridocyclitis, choroiditis, and optic and retrobulbar neuritis. Many of the latter used to lead to blindness in presteroid days. Today, when intraocular inflammations are treated adequately with large doses of steroids over a sufficient length of time, a high percentage of beneficial results are secured, and the patients often are saved from blindness. Dexamethasone has the advantage of functioning by the oral route and thus can be used in the treatment of severe intraocular infections in ambulant patients. I have a number of patients with chronic uveitis in their only eye or in both eyes who, in presteroid days, undoubtedly would have become blind. Today many of them are managed satisfactorily on an ambulatory basis with systemic dexamethasone therapy.

From the New York Hospital, Cornell Medical Center, and the L. Margolyes League.

Read before the Section on General Practice at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

Dexamethasone is not completely free from the side-effects common to the corticoids, and hence is not the ultimate answer in steroids. However, it is a superior anti-inflammatory and antiallergic drug which, when used properly, gives a very high percentage of successful results. I have not encountered any serious side-effects in patients who have been treated only with dexamethasone during the entire course of their illness. There have been some cases of water retention but not of great magnitude. These patients have responded to therapy with chlorothiazide and meralluride (Mercuhydrin) sodium given by the intramuscular route.

Summary and Conclusions

Dexamethasone is a superior form of steroid when used systemically or topically in the treatment of external ocular and intraocular inflammations. The indications for dexamethasone therapy in ophthalmology are inflammation, allergy, edema, granulation tissue, and certain infections. In the latter, the concomitant use of antimicrobial therapy is mandatory. The contraindications to use of dexamethasone, in addition to the usual systemic contraindications to use of any of the steroids, are herpes simplex keratitis, fungal keratitis, and certain exanthematous involvements of the cornea. Steroid therapy has revolutionized the treatment of intraocular inflammations. In this connection dexamethasone has proved to be a most potent agent.

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The bulk of the orally administered dexamethasone and all of the topically administered dexamethasone used in this study were supplied as Decadron through Dr. N. Capeci of Merck Sharp & Dohme, Philadelphia. Additional dexamethasone was supplied as Deronil through Dr. H. Pifer of the Schering Corporation, New York.

ENDOSCOPIC ASPECTS OF ESOPHAGITIS AND ESOPHAGEAL HIATAL HERNIA

Paul H. Holinger, M.D., Chicago

Esophagitis, an inflammation of the esophageal mucosa, is most commonly seen at the cardia and immediately above it and is generally most severe in the distal esophagus. It may involve the entire esophageal mucosa or only localized patches. When it is found in isolated parts of the esophagus, biopsy has shown gastric mucosa in the wall of the esophagus, even at the levels above the arch of the aorta. Diffuse esophagitis involving the entire extent of the esophagus is seen in alcoholics. Varying degrees of inflammation are seen in patients with caustic burns, in debilitated patients whose conditions are associated with frequent vomiting or regurgitation, and in patients with cardiospasm, in whom esophageal retention results in fermentation of food. Occasionally patients who have had a nasogastric feeding tube in place for a long period of time develop inflammation and ulceration in the cervical esophagus and at the cardia. Esophagitis is often most intense postsurgically in patients who have had a partial esophageal resection for a benign or a malignant esophageal stricture. The inflammation is severest at and around the site of anastomosis.

Types of Esophagitis

Acute esophagitis is a frequent disease in infants and children. It may occur as an associated condition in cases of infectious fevers and as a complication of other esophageal diseases, with intrinsic obstruction or with a foreign body. Inflammatory changes are found in the distal part of the esophagus of infants as a result of reflux of gastric juice, from either congenital dysfunction of the esophagogastric junction or persistent vomiting. The symptoms are due to esophageal spasm, which may be reflected in the esophagram as a constriction of varying length and will be noted esophagoscopically in the abnormal redness of the mucosa. Superficial ulceration may be seen, and the tissues bleed easily on contact with the instruments. Esophagitis is characterized by mucosal edema, hyperemia with intense redness of the mucosa, superficial erosion, and even deep, penetrating ulceration. The mucosa oozes readily on contact with the examining esophagoscope, and granulation tissue may be seen which cannot be distinguished from a neoplasm except

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by biopsy. Early in the course of the disease the esophageal walls are usually soft, but if the process has been a long-standing one the esophageal wall may be thickened and rigid, with areas of moderate to severe stenosis. Stenosis, particularly at the cardia, is often associated with rigidity and patency of the stenotic opening that permits a free back-and-forth flow of gastric secretions. This increases the severity of the condition by failure to retain the gastric juice in the stomach and promotes the formation of penetrating ulcers and persistent hemorrhage.

A second type of esophagitis of an entirely opposite appearance is the atrophic esophagitis associated with Plummer-Vinson syndrome and with pernicious anemia. Patients, almost always women, with this condition complain of dysphagia, a lump in the throat, and often a desire to swallow frequently or even a need to swallow two or three times before the swallow seems to be effective. While the blood studies confirm or assist in establishing the diagnosis, esophagoscopy reveals the mucosal changes. The esophageal walls have a pale, paper-thin appearance, usually dry on the surfaces and exceedingly smooth and glossy. This is frequently in marked contradistinction to the beefy red appearance of the smooth tongue in such patients. Stenosis, particularly of the upper esophagus where the changes are first noted, may be marked. A high percentage of patients develop neoplastic changes.

Hiatal Hernia

Hiatal hernia shows a variable picture. In patients with the sliding type, findings may be negative, particularly if herniation occurs only with the severest lifting or straining. When gastric mucosa remains in the thorax, fluid retention in the esophagus and in the supradiaphragmatic stomach are seen. Under these circumstances, esophagitis is found at the esophagogastric junction. The esophageal mucosa is relatively smooth in contradistinction to the red, velvety gastric mucosa below. Distinct color and texture changes designate the level of the cardia well above the expected measurement of the diaphragmatic level.

Obstruction to swallowing is rarely absent in patients with hiatal hernia. When the herniation of a portion of the stomach is not associated with shortening of the esophagus, obstruction is caused by kinking at the cardia; obstruction may occur when the supradiaphragmatic portion of the stomach is isolated by constriction of the hiatus or the diaphragmatic crura. In hiatal hernia associated with shortening of the esophagus, an extreme degree of stenosis is often found. The stenotic lumen may be kinked, tortuous, and rigid, with a high degree of fibrosis, or the stenosis may consist merely of a tough, membranous web. Secretions are retained above the cardia, in [illegible] portion of the stomach, or, [illegible] diaphragmatic portion of the stomach to be forced back upward because of an associated pyloric obstruction. Ulceration, bleeding, granulation tissue, and edema characterize the appearance of the esophageal walls immediately above the constriction. Benign ulcers are difficult to differentiate from malignancy, and, in fact, malignant change is not uncommon in ulcers either above or below the constricted cardia.

Indications for esophagoscopy in patients with esophagitis and hiatal hernia are both diagnostic and therapeutic. In patients with symptoms of epigastric and substernal pain, dysphagia, regurgitation, and occasional tarry stools, esophagoscopy is indicated whether x-ray findings are definite or inconclusive.

Pain radiating to the back in association with other esophageal symptoms usually suggests a penetrating ulcer and carries a more serious prognosis. An evaluation of esophageal, supradiaphragmatic gastric, and subdiaphragmatic retention may be made to assist in determining the therapeutic program.

From a therapeutic standpoint, much can be gained by endoscopic dilatation of stenoses. If the fibrosis is severe, this may have to be done over a previously swallowed thread; if the esophagoscopic examination shows the stenosis to be soft, the use of mercury-filled rubber bougies is most effective.

Repeated examinations serve to determine the effectiveness of the various therapeutic procedures, particularly the postsurgical course, if surgery has been necessary.

Summary

Edema, hyperemia, and superficial ulceration characterize the endoscopic changes of esophagitis. In some cases, deep ulceration, rigidity, and stenosis require biopsy. Esophagitis may be encountered at any level in the esophagus but is most commonly seen in the distal one-third. It is often associated with aberrant gastric mucosa, even when seen above the midesophagus.

Hiatal hernia gives a variable picture. In patients with the sliding type, findings may be negative. When gastric mucosa remains in the thorax, fluid retention in the esophagus and supradiaphragmatic stomach are seen. The cardia measures above the diaphragmatic level. Stenosis at the cardia and diaphragm is associated with esophagitis. Fibrosis and a fixed open lumen allows a free to-and-back flow of gastric secretion between stomach and esophagus. Repeated examinations are desirable to evaluate the effectiveness of therapy.

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CLINICAL FEATURES IN THE MANAGEMENT OF ESOPHAGEAL HIATAL HERNIA

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A hernia about the esophageal hiatus of the diaphragm affects the junction of the esophagus and the stomach in various ways, and the results can be classified either anatomically or clinically. Anatomically (roentgenographically) there are two types—the sliding and the rolling. Clinically (symptomatically) there are five types—those without symptoms, those with substernal or abdominal distress, those with gross or occult bleeding, those with dysphagia, and those with associated peptic ulcer. Complications such as stricture and hemorrhage are most common when ulcer of the stomach or duodenum coexists with hiatal hernia. Conservative measures, including bougienage, have generally proved satisfactory.

Notable advances have taken place in our understanding of the problems of hiatal hernia in recent years. This newer knowledge has had an important influence on the medical and surgical management of patients with this disorder. It is now well recognized that inflammatory changes in the distal part of the esophagus are often present in patients with hiatal hernia. The esophagitis is attributed to the regurgitation of gastric juice into the lower esophagus.[1] Numerous workers have shown that gastroesophageal reflux occurs frequently in many patients with hiatal hernia. The reflux is attributable to several factors. The sphincteric mechanism at the distal end of the esophagus may be impaired.[2] The angle of junction of the stomach and esophagus is also considered to exert a valve-like action which opposes regurgitation, and this function may be lost in patients with hiatal hernia.[3] Relaxation of the muscle fibers at the diaphragmatic hiatus is probably of less importance.

New methods for the repair of hiatal hernia have been devised by Allison[3] and others. These have the purpose not only of restoring normal anatomy but also of correcting the factors which permit gastroesophageal reflux. As a consequence of the better understanding of esophagitis and of improvements in surgery, a larger number of patients with hiatal hernia are now being considered for surgical repair. Belsey[4] predicted in 1952 that a trend would be established toward a freer use of surgery, until we have acquired sufficient experience to be able to offer a more accurate prognosis in an individual patient. At the present time it appears that there is a considerable divergence of opinion about the indications for surgical intervention in this disease. Some authors state that most patients with hiatal hernia tend to have few, if any, symptoms and, hence, that surgical repair is not frequently indicated. Others emphasize the seriousness of some of the complications of hiatal hernia, such as stricture and hemorrhage, and believe that a tendency toward progressive disability in patients with this disease justifies an aggressive therapeutic approach.

It seems important, therefore, to attempt to summarize our present knowledge concerning prognosis in patients with hiatal hernia. If possible, the risk of the development of important complications in the individual patient should be defined. Those patients who may be destined to develop complications should perhaps be considered for surgical repair. The potential seriousness of esophagitis as a complication needs particular clarification.

Classifications of Hiatal Hernia

Hiatal hernias may be classified on either an anatomic or a symptomatic basis. The anatomic classification of Åkerlund, modified by Allison,[3] divides most cases of hiatal hernia into two main groups, the sliding and the rolling varieties. In the *sliding variety*, the cardiac end of the stomach slips upward through the diaphragmatic hiatus, tending to leave the peritoneal covering of the stomach below the diaphragm. In the rolling type, a portion of the fundus covered by peritoneum tends to slip upward through the diaphragm lateral to the esophagus. Frequently both of the above types of upward movement of the cephalic portion of the stomach occur and the hernia is actually a mixture of the two types.

The anatomic classification of hiatal hernia is suggested by the roentgenographic appearance. In the typical sliding hernia, the junction of the esophagus and stomach is located at or near the apex of the [illegible] gastric pouch in the chest, whe[illegible]ype a lateral angle of entry of the esophagus into the stomach is preserved. The clinical importance of this distinction lies in the fact that gastroesophageal reflux and esophagitis are less prone to occur in patients with the rolling

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than in those with the sliding type of hernia.[4] However, reflux and esophagitis can occur, according to some observers,[5] in an appreciable number of patients with the rolling type of hernia as well as in those with the sliding type.

The practical usefulness of an anatomic classification of hiatal hernia is somewhat limited. Johnstone[6] has pointed out that only a surgeon can establish with certainty whether a hernia is sliding or paraesophageal in type. This differentiation is difficult to be certain about on the basis of roentgenologic study.

Clinical analyses of hiatal hernia are based primarily on a classification of patients in terms of the predominating symptoms.[7] The chief symptomatic groups, in order of frequency, of patients with this disease may be summarized as follows: (1) the group of patients with no symptoms; (2) that of patients with substernal or abdominal distress; (3) that of those with hemorrhage, including both gross hemorrhage and occult bleeding with anemia; (4) that of those with dysphagia, caused by esophageal stricture, esophagitis with spasm, or other causes; and (5) that of those with associated ulcer of stomach or duodenum, which last group merits special consideration. Perforation or strangulation are rare complications. It will be seen that, as is the case in patients with ordinary peptic ulcer, patients can be classified as those whose symptoms are limited chiefly to pain and distress and those with complications.

Uncomplicated Hiatal Hernia

The frequency with which gastrointestinal symptoms may correctly be attributed to hiatal hernia is a matter concerning which there is considerable divergence of opinion. Hiatal hernia may be essentially asymptomatic.[8] Some authors report that the proportion of asymptomatic patients is large. While hiatal hernia may be an asymptomatic finding, it is common experience that patients with this disorder may complain of a variety of types of substernal or abdominal distress. On the basis of extensive observation Harrington[9] pointed out that the symptoms of hiatal hernia may mimic the clinical picture of other abdominal disorders and labeled hiatal hernia as the "masquerader" of the abdomen.

It appears that the major types of discomfort which are referable to hiatal hernia fall into two main groups. Allison[3] vividly described the pattern of symptoms which seem to be related to the esophagus and to the phenomenon of gastroesophageal incompetence. These symptoms include heartburn, substernal pain, and a sense of regurgitation, which are often brought about by lying down or bending forward. The heartburn is characteristically a sensation of burning under the sternum, which often seems to radiate upward from the region of the xiphoid process. Other patients complain of distress which may be more directly related to the hernia. Episodes of sharp or dull lower substernal or upper abdominal pain may take place. This type of distress often seems to originate in direct relation to the hernia, although methods are not currently available which permit a critical distinction to be made between symptoms of esophageal origin and symptoms arising from the hernia per se. The pain in hiatal hernia may also be of a type which is difficult to distinguish from cardiac pain.

The long-term clinical course of patients with hiatal hernia has been a subject of follow-up study in one series of patients at the Presbyterian Hospital.[10] The clinical course of the average patient with substernal or abdominal pain attributable to hiatal hernia, but without complications, tends to be relatively benign. Although the symptoms are often persistent or tend to recur, they usually remain mild and the patients frequently experience long asymptomatic periods under medical management. Complications have not arisen frequently during follow-up in patients with pain or distress who were initially free from complications. In a series of 56 patients who have been observed under conservative therapy for an average period of four years and seven months only 5 patients have thus far developed any complications, including 2 who had an episode of gross hemorrhage. Three patients developed dysphagia attributable to esophagitis with spasm, and one of these also had an episode of incarceration of the hernia which necessitated surgical intervention. These observations support the view that the clinical course in patients with uncomplicated hiatal hernia is usually benign. A few of these patients will develop such complications as hemorrhage or obstruction. To determine whether a substantial number of patients will develop complications after a longer period of time requires a longer period of follow-up observation.

Esophagitis which is visible at esophagoscopy may be present in patients whose only important symptom is heartburn or some other type of substernal or epigastric distress. The gross characteristics of the esophagitis include hyperemia of the mucosa in the distal esophagus, associated, at times, with edema and a tendency to bleed, with trauma. Superficial ulceration may occur. The presence of the esophagitis does not necessarily signify an unsatisfactory prognosis. Changes of this type were seen in 6 of 16 of the patients in the above-mentioned series on whom esophagoscopic examination was performed. No significant difference was observed in the subsequent clinical course in this small group. Patients who were known to have had esophagitis early in the course of follow-up observation did not become progressively worse.

A small proportion of patients with uncomplicated hiatal hernia suffer from unremitting and relatively severe heartburn or substernal or epigastric pain. Study of a group of such patients[10] revealed that inflammatory changes in the esophagus were present in some patients but were usually mild in intensity. Frank ulceration of the esophagus has occasionally appeared to explain severe pain. A considerable number of the patients with pain or severe heartburn which recurred daily for many months or years have exhibited no evidence of esophagitis on esophagoscopic examination. At operation, some patients of this type have been found to have periesophagitis, which may have been a factor in the production of symptoms. In some patients an associated state of tension appears to play a role.

Hiatal Hernia with Hemorrhage

Hemorrhage as a complication of hiatal hernia usually occurs as an episode of gross blood loss. The bleeding may be profuse and shock may supervene. However, death due to hemorrhage in patients with hiatal hernia without an associated peptic ulcer has seldom been reported and apparently is quite rare. Gross hemorrhage may be expected to recur in at least one-third of patients with hiatal hernia who have previously bled. In the long-term study,[10] 8 of 21 patients who suffered from gross hemorrhage had more than one episode of bleeding.

The site of bleeding is probably the lower part of the esophagus in some patients. Clerf and coworkers[11] found ulceration at the cardioesophageal junction on esophagoscopic examination of a series of patients who had had hemorrhage. Frequently no visible source of bleeding can be found at esophagoscopy or gastroscopy in patients who have had an episode of bleeding. It has also been suggested that bleeding may, at times, be due to congestive or inflammatory changes in the herniated portion of the stomach. Presumably such a process can be transitory and therefore may not be demonstrated on endoscopy unless the examination is carried out soon after the hemorrhage.

Anemia due to occult bleeding in patients with an otherwise asymptomatic hiatal hernia is a less common type of problem.[12] It is more often associated with large than with small hernias. The reason for this is not apparent, and, in fact, the site of blood loss is not always demonstrable by roentgenologic and endoscopic techniques. Anemia of this type can usually be corrected by the administration of iron.

Hiatal Hernia with Dysphagia

Dysphagia, a sense of stoppage during the swallowing act, may be produced by a variety of mechanisms in patients with hiatal hernia. The obstruction may occur at the lower end of the esophagus. It may be due either to stricture or to motor dysfunction resulting from esophagitis. Delayed emptying of food from the herniated portion of the stomach through the diaphragmatic hiatus may also cause dysphagia.

Esophagitis with Stricture.—Stricture of the esophagus above a hiatal hernia is revealed on roentgenography, bougienage, and esophagoscopy. X-ray examination reveals narrowing of the lumen of the distal esophagus. Bougienage with a semiflexible bougie reveals a point of fixed obstruction at the level of the stricture. Esophagoscopic examination will confirm the presence of the stricture.

Case 1.—A 65-year-old man was found to have a large hiatal hernia of the sliding type, in 1950, by roentgenography, in the course of investigation for symptoms due to carcinoma of the colon. He had had no previous symptoms referable to the upper part of the gastrointestinal tract. A partial colectomy was performed, with removal of an adenocarcinoma of the colon. Intubation with a nasogastric tube was necessary for a number of days postoperatively. During the postoperative period the patient developed dysphagia for solid foods. Bougienage revealed a point of obstruction located about 35 cm. below the gum margin. Esophagoscopic examination disclosed superficial ulceration in the distal esophagus, with stricture formation.

Accordingly the patient was treated by means of weekly dilations with metal bougies and an ulcer type of dietary regimen. Bougienage was continued until a maximum diameter of 40 French was reached, two months after the onset of treatment. There was complete relief of symptoms for three years, after which time there was a recurrence of mild dysphagia. Esophagoscopy was then repeated and again revealed esophagitis, but no stricture was present. During the succeeding six years the patient has been free from upper gastrointestinal symptoms except for occasional mild dysphagia.

The history of this patient illustrates the fact that the symptoms of stricture of the esophagus may appear abruptly. Many patients with stricture do not have a long history of gradually developing dysphagia.[13] The history often suggests that scarring has occurred rapidly and may have followed an episode of acute ulceration. Stricture resulting from gradually progressive inflammatory changes in the esophagus is more difficult to document, and it is not clear how often it occurs.

The stricture of the esophagus which is associated with hiatal hernia is soft and is readily stretched by appropriate bougienage. After full dilation occasional episodes of dysphagia may still occur. As a rule, these are readily relieved by repeated treatment. Occasionally dilation of a stricture is technically impossible, and surgical intervention may become necessary.

Esophagitis with Spasm.—A similar clinical picture may occur in patients with esophagitis and hiatal hernia without stricture. Roentgenography in patients with this type of hiatal hernia may also reveal a narrow lumen in the distal end of the esophagus; however, on bougienage no fixed obstruction is encountered, although palpation may reveal a sense of diffuse spasm. Recently motility studies have suggested that propulsive peristalsis may be disrupted over a considerable distance in the lower esophagus.[14] Esophagoscopic examination commonly reveals inflammatory changes with or without ulceration.

CASE 2.—A 56-year-old woman was first seen in 1953, complaining of heartburn and substernal pain of nine years' duration and episodes of dysphagia of seven years' duration. A large hiatal hernia was visualized on x-ray examination. Esophagoscopy revealed shallow ulceration at 54 cm. Silk bougies were passed and a mild dragging sensation was encountered in the distal end of the esophagus. However, a 38 French bougie could readily be passed into the stomach. Therapy was instituted which included an ulcer type of regimen and periodic bougienage with silk bougies. The patient was largely free from symptoms for four years, after which time mild dysphagia recurred. Examination by bougienage at this time suggested that some scarring, with stricture formation, had occurred. Occasional dilation of the stricture with metal bougies has since been required in order to keep the esophagus patent.

This patient was considered to be suffering from dysphagia due to disordered motor function in the distal part of the esophagus. No evidence of stricture was apparent for four years. Patients of this type, who suffer from some dysphagia due apparently to esophagitis without stricture, are prone to continue to have mild intermittent dysphagia under medical management. However, progression of the disorder with the development of stricture is unusual.

Dysphagia Due to Other Causes.—About one-half the patients with hiatal hernia who complain of dysphagia present no evidence on routine study that definitely indicates that the site of obstruction is at the lower end of the esophagus. Roentgenography, bougienage, and esophagoscopy fail to reveal any narrowing or obstruction in the lower esophagus. Some degree of esophagitis may or may not be present and may play a role. In other instances the history suggests that the dysphagia may be due to an inability to empty the supradiaphragmatic stomach pouch.

CASE 3.—A 54-year-old woman was first seen in 1955, complaining of attacks of dysphagia and vomiting for two years. Five years earlier, after a hysterectomy, she began to suffer from substernal pressure which came on shortly after meals. Three years after the onset of symptoms she began to have occasional attacks of complete inability to swallow, accompanied by nausea and retching and requiring narcotics for relief. On one occasion the patient vomited a moderate amount of red blood. Roentgenologic examination revealed a large rolling type of hiatal hernia, with about half of the stomach in the chest. A flexible bougie was passed into the stomach without meeting obstruction. Esophagoscopy and gastroscopy showed no inflammatory changes in the esophagus or herniated portion of the stomach. Because of the severity of the attacks of dysphagia, surgical repair of the hiatal hernia was recommended. At operation, the hernia proved to be a combination of the sliding and rolling types.

It seems likely that dysphagia of the type described in this patient is due to obstruction occurring in the hernial pouch at the level of the diaphragmatic hiatus. The fact that this may occur is best shown by the fact that roentgenologic examination occasionally demonstrates an impaction of food in the supradiaphragmatic portion of the stomach in patients with an attack of dysphagia.[10]

Some patients with hiatal hernia and dysphagia have a contractile ring at the lower end of the esophagus.[15] The exact nature of the ring is at present unknown. According to Schatski and Gary, a contractile ring is not associated with dysphagia unless the diameter is less than 13 mm.

Hiatal Hernia and Peptic Ulcer

Patients who have both hiatal hernia and peptic ulcer present a special problem. Many such patients suffer from esophagitis. The importance of the triad of peptic ulcer, hiatal hernia, and esophagitis was emphasized by Benedict and Sweet,[16] who studied a series of such patients who had developed a stricture of the esophagus. Winkelstein and others[17] emphasized the comparatively unfavorable prognosis of patients who have ulcer of the stomach or duodenum and esophagitis, with or without hiatal hernia.

In a group of 27 patients with hiatal hernia and peptic ulcer,[10] the ulcer was located in the duodenum in 22 patients, in the stomach in 4 patients, and in the jejunum in one patient who had previously had a subtotal gastrectomy. Symptomatic complications were frequent in this group. Of a total of 27 patients there were only 10 whose sole symptom was distress; 11 had hemorrhage; and 14 had dysphagia, due in 4 to stricture, in 5 to esophagitis with spasm, and in 5 to other causes. Of the 27 patients 17 had either gross hemorrhage or dysphagia or both.

The high incidence of complications in patients with hiatal hernia and peptic ulcer is partly attributable to esophagitis. In the above series of patients, dysphagia was attributable to esophageal disease in 9 of the 14 patients who had difficulty in swallowing. Of the 11 patients who bled, 8 were found at esophagoscopy to have inflammatory disease of the lower esophagus. The esophagus was, therefore, considered to be a potential source of hemorrhage, although it was impossible to be certain of the exact site of bleeding in most instances. The frequency of esophagitis in patients with ulcer and hiatal hernia has been ascribed to the so-called peptic diathesis. Hypersecretion of gastric juice may be a factor in the development of esophagitis in such patients.

Prognostic Significance of Esophagitis.—Esophagitis is the immediate basis for many of the symptomatic complications of hiatal hernia. It is probably the most frequent cause of dysphagia and it is frequently the apparent origin of hemorrhage. These facts suggest the possibility that the presence of esophagitis in patients with hiatal hernia should be interpreted as a bad prognostic sign. However, it is not clear at present how often esophagitis in association with hiatal hernia tends to become chronically progressive.

Mild inflammatory changes such as reddening, friability, and edema in the lower part of the esophagus may be rapidly reversible and may disappear within a few weeks under appropriate medical treatment. The presence of mild esophagitis in patients who have not suffered from symptomatic complications of hiatal hernia has not been shown to be a bad prognostic sign. In fact, esophagoscopic examination in patients with uncomplicated hiatal hernia has, in a limited experience, been disappointing as a procedure to help determine prognosis.

Chronic esophagitis with stricture formation often appears to develop rapidly. The rapidity with which scarring of the lower part of the esophagus may occur is frequently suggested by the fact that the duration of dysphagia as a symptom has been brief when the presence of a stricture is first recognized. Chronic esophagitis in which there has not been a sudden symptomatic onset is encountered in some patients with dysphagia. Esophagoscopic examination may reveal either scarring or spasm of the lower part of the esophagus. There appear to be few data on the frequency of chronic progressive esophagitis in patients with hiatal hernia without dysphagia.

Summary and Conclusions

The recent improvements in the surgical approach to the problem of hiatal hernia have made it desirable to review the natural history of this disease and to attempt to improve our criteria for the selection of those patients whose outlook under medical management is poor. Available evidence favors the view that the average patient with hiatal hernia has a small statistical likelihood of developing the complications of the disease under conservative management. In one series[10] about 10% of patients developed complications during a follow-up period of almost five years. Some of the patients with uncomplicated hiatal hernia who have relatively severe and persistent distress under medical management form a special group. No single factor underlies this type of relative intractability.

Gross hemorrhage in patients with hiatal hernia may be severe but is seldom fatal. It tends to recur in over one-third of the patients who bleed. In this respect the problem of recurrent hemorrhage seems similar to that of duodenal ulcer with hemorrhage.

Dysphagia in patients with hiatal hernia may be due to scarring or disorganized motor behavior in the lower part of the esophagus. At the present time no criteria are available whereby the patients with uncomplicated hiatal hernia who are destined to develop dysphagia due to esophagitis can be selected. However, the results of conservative therapy, including bougienage, in patients with hiatal hernia with esophageal stricture or spasm are usually quite satisfactory. Dysphagia may also occur in patients with hiatal hernia as a result of impaired emptying of the supradiaphragmatic stomach pouch. Surgical intervention may be indicated for relief of symptoms in such patients.

Patients who have both hiatal hernia and peptic ulcer present the highest incidence of such complications as hemorrhage and stricture. Esophagitis develops more frequently in such patients than in those with hiatal hernia alone. While some patients with both hiatal hernia and peptic ulcer have a satisfactory clinical course under conservative management, a number of such patients may merit consideration for some type of surgical intervention.

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ROLE OF MOTILITY PATTERNS IN THE DIAGNOSIS OF ESOPHAGEAL DISEASE

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In patients with various types of substernal and thoracic pain or with unusual types of dysphagia, the study of esophageal motility has been valuable in directing the treatment. Three case histories bear out this statement. In two patients (a woman 69 and a man 66 years of age) increasingly severe dysphagia led to studies of esophageal motility and ultimate surgical correction. In the third case a man aged 41 years had repeated episodes of substernal pain which at first suggested heart disease, but studies of esophageal motility, together with negative cardiologic findings, clearly showed that the patient's substernal pain was related to abnormal esophageal contractions. Since anxiety and tension were major factors in his condition, the exclusion of heart disease from the diagnosis was doubly significant.

The diagnosis of organic lesions of the esophagus usually can be made by conventional methods. Most obstructive lesions of the esophagus can be recognized by roentgenographic examination after the patient has swallowed a contrast medium such as barium sulfate. Esophagoscopic examination is likewise of great importance in the recognition of esophageal disease. As a rule, the nature of the disorder is suspected on direct inspection of the interior of the esophagus, and, in the case of malignant disease, the examination of biopsy specimens will confirm a diagnosis already suspected by the roentgenologist and the esophagoscopist.

The diagnosis of disturbances of function of the esophagus is often difficult when the patient does not have symptoms of esophageal obstruction. This is especially true in the early phases of such disturbances as achalasia, diffuse spasm of the esophagus, and even esophageal hiatal hernia. The barium passes through the esophagus so rapidly that the roentgenologist may not recognize the nature of the disturbance unless he exercises great care and uses special techniques. By the same token, esophagoscopy may reveal little unless there is organic obstruction or definite changes in the mucosa of the esophagus. In fact the endoscopist at times may learn more from the passage of bougies over a previously swallowed thread than from actual inspection of the interior of the esophagus.

In recent years, studies of esophageal motility have added a great deal to our knowledge of the functional disturbances of the esophagus. A number of techniques for recording esophageal motility have been described,[1] but all depend on the measurement of pressures within the esophagus and at

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its sphincters. Of particular value has been the simultaneous measurement of pressures at various levels during the act of deglutition. In the clinic laboratory, pressures have been measured with the aid of tiny electromagnetic transducers. The exact techniques have been described in detail in other publications, and patterns of motility have been established for the normal esophagus and for such disorders of this organ as achalasia, diffuse spasm, and scleroderma.[2] In addition, some progress has been made in the understanding of other esophageal disorders, including esophageal hiatal hernia. This technique has been so valuable in the diagnosis of nonobstructive and nonorganic disturbances that it has become almost routine as a supplement to roentgenographic and esophagoscopic examinations.

In the early phases of our investigations it was quite natural that we should attempt to determine the motility patterns that might have been seen in a previously recognized clinical syndrome or disorder. In these early cases, the clinical diagnosis had already been made and the motility pattern must perforce match the clinical diagnosis. As we gained experience it became evident, however, that we were relying more and more heavily on the pattern of esophageal motility as the final criterion of diagnosis. Likewise, we have learned that not all patients with achalasia, for example, had exactly the same motility pattern, and, by the same token, considerable variation has been noted in patients whose patterns were included in the category of diffuse spasm. In some instances we have obtained records which show a combination of features previously ascribed to either achalasia or diffuse spasm. In fact, it seems probable that a number of new entities will emerge as these various disturbances of function are studied more carefully. Furthermore, studies of esophageal motility have proved to be of great value in the clinical assessment of patients with various types of substernal and thoracic pain and of patients who have unusual types of dysphagia.

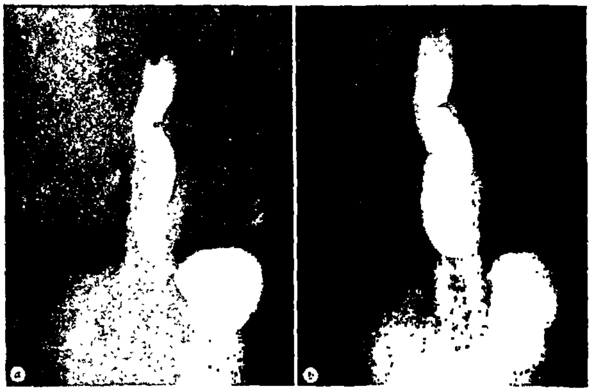

Fig. 1 (case 1).—Achalasia of esophagus. *a*, Evidence of simulated diffuse spasm of esophagus is shown on roentgenogram made Jan. 10, 1956. *b*, Progressive dilatation is evident on roentgenogram made Feb. 20, 1957.

We realize that a great deal of further investigative work must be done before too much reliance can be placed on the value of these pressure studies in the diagnosis of unusual syndromes. Nevertheless, we should like to call attention to certain instances in which the study of motility has been of great value in directing the treatment of the patient. Some pertinent cases encountered at the Mayo Clinic will be illustrative.

Report of Cases

Case 1.—A woman, 69 years of age, was seen in January, 1956. Since the death of her husband three years previously she had been somewhat nervous. During the three months prior to coming to the clinic she had had two episodes of choking. Both episodes had occurred at the dinner table and both were followed by an unusual amount of salivation. After the second choking spell her family induced her to have a roentgenogram made of the esophagus and, hence, she reported for examination. Careful interrogation revealed that she had had occasional choking spells over many years but she denied having any such trouble within the preceding five years until the recent episodes. She also denied any difficulty in swallowing, although members of her family stated that she ate slowly and was inclined to avoid meats.

The roentgenogram showed what appeared to be a mild diffuse spasm (fig. 1*a*) and the possibility of a small hiatal hernia was raised. An esophagoscopic examination was performed but the results were essentially negative. However, when 41 and 50 French sounds were passed over a previously swallowed thread, it was felt that there was more than the usual resistance at the cardia. Her symptoms were minimal and because of this nothing further was done.

A year later, in February, 1957, the roentgenographic study of the esophagus was repeated and the appearance was more suggestive of achalasia (fig. 1*b*). At this time the patient underwent esophageal motility studies. It was obvious that there was complete motor failure of the esophagus (fig. 2). No peristaltic contractions were evident. Small, feeble, simultaneous contractions were noted in the lower part of the esophagus. A fairly high pressure was noted within the gastroesophageal sphincter while the patient was at rest. In contrast to the behavior of the sphincter in patients with usual achalasia, relaxation of the sphincter in this patient took place after swallowing and was followed by a vigorous and prolonged contraction. The methacholine (Mecholyl) chloride test gave positive results. Despite evidence of motor failure, the tracing was not typical of achalasia because the lower sphincter did open in response to the swallowing effort. Hence, this actually might be called "achalasia without achalasia," inasmuch as the term "achalasia" means "failure to open." On the basis of the motility study, we thought we were dealing with atypical cardiospasm or achalasia. In any case, we knew that there was a real basis for the patient's difficulties and that they certainly were not imaginary. Subsequently, 41 and 50 French sounds were passed, with the typical findings of achalasia. The patient still considered her symptoms minimal and did not wish further treatment.

Nearly two years later she fell and broke the neck of her right femur. Surgical treatment was necessary and she was confined to bed for several weeks. During this time it became obvious that severe difficulty with swallowing was developing. Roentgenograms appeared similar to those made in 1957 (fig. 1*b*). On Jan. 27, 1959, left-sided thoracotomy was performed and the lower end of the esophagus was exposed. The lower sphincter was greatly hypertrophied and esophagomyotomy of the Heller type was performed, which necessitated an excision that extended 5 cm. up the esophagus and about 2 cm. on to the stomach. The patient had an uneventful convalescence and has not had difficulty swallowing since that time.

In this case, studies of esophageal motility established the fact that the patient had motor failure of the esophagus. In contrast to patients with usual achalasia, in this patient the sphincter did relax with swallowing but this relaxation was followed by a powerful contraction. In any case, the study of motility demonstrated that the patient's problem was not psychosomatic and certainly not a problem of diffuse spasm. The relatively powerful contraction that followed the initial relaxation of the lower sphincter suggested to us that treatment by surgical myotomy would be wiser than treatment by hydrostatic dilatation. The findings at operation confirmed our impressions in this case. Furthermore, this case suggests that not all patients with motor failure of the esophagus have associated achalasia of the cardia. There is need for more accurate terminology in this group of conditions.

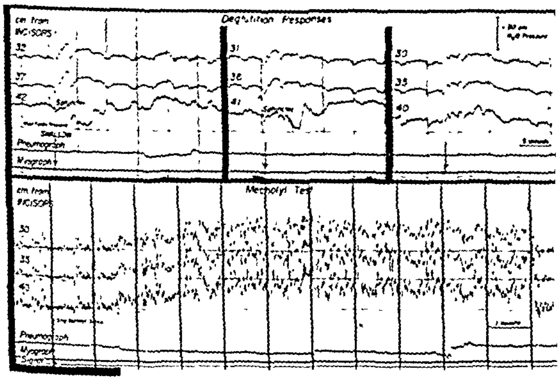

Fig. 2 (case 1).—Atypical achalasia. *Upper left*, evidence of feeble simultaneous contractions of lower portion of esophagus after deglutition, with sphincter relaxed (42 cm. from incisor teeth); *upper middle*, same, with sphincter at 41 cm.; *upper right*, feeble simultaneous responses to swallowing, with three units in esophagus; *bottom*, positive response to injection of methacholine (Mecholyl) chloride.

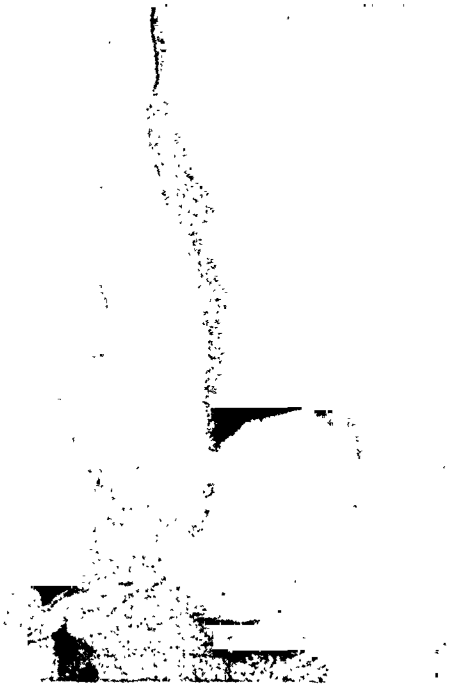

Fig. 3 (case 2).—Pulsion diverticulum of the esophagus. Roentgenogram also suggests presence of small hiatal hernia.

CASE 2.—A 66-year-old man registered at the clinic on March 19, 1959. He had been under treatment for auricular fibrillation since 1946 and could usually control his cardiac irregularity with quinidine. In November, 1958, after an episode of auricular fibrillation, he began to regurgitate all of his food. Roentgenographic studies of the esophagus at that time showed a pulsion diverticulum of the lower part of the esophagus. Between October, 1958, and March, 1959, the diverticulum had doubled in size. He was referred to us for surgical removal of the diverticulum.

Our roentgenograms showed a rather large epiphrenic diverticulum (fig. 3). Because of experiences with previous cases, we suspected that his difficulties might not be related entirely to the diverticulum. Therefore, studies of esophageal motility were suggested. These were carried out and the findings are recorded in figure 4. The diverticulum itself would not have been detected on the basis of these tracings; however, it was obvious that the patient had complete motor failure of the esophagus, with classic signs of achalasia. The motility studies as well as the x-ray examination indicated the presence of a small hiatal hernia.

The diagnosis of hiatal hernia was based on the "double reversal" of the pressure waves in relation to inspiration and expiration and on the presence of a broad zone of elevated pressure above the esophageal hiatus.

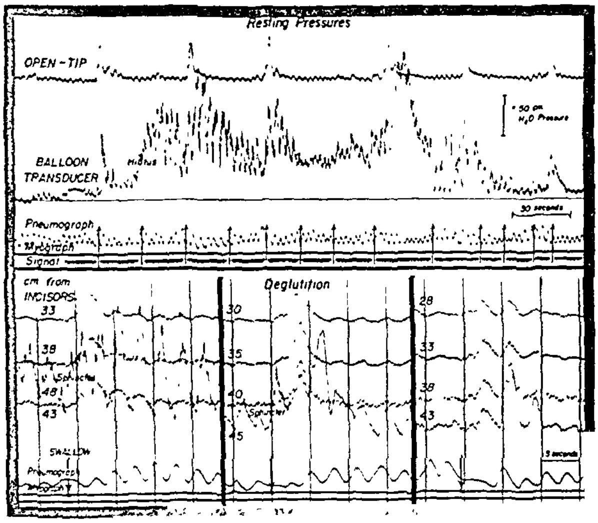

Fig. 4 (case 2).—Motility studies, showing classic signs of hiatal hernia and achalasia. *Top,* resting pressures at esophagogastric junction (lower tracing), showing broad band of high pressure and "double reversal" phenomenon of hiatal hernia; *bottom,* tracings from lower part of esophagus and sphincter, showing marked elevation of pressure and failure of sphincter to relax—tracings diagnostic of achalasia.

On March 26, 1959, left-sided thoracotomy was done and the lower portion of the esophagus was mobilized. The findings were typical of cardiospasm and a small hiatal hernia of the sliding type was present, with approximately 4 cm. of stomach above the diaphragm. The epiphrenic diverticulum was dissected out and removed. Esophagomyotomy of the Heller type was performed and the hiatal hernia was then repaired. The patient's recovery was completely satisfactory and he was entirely relieved of his dysphagia.

Our experience with pulsion diverticula of the lower part of the esophagus would indicate that the greatest number of these diverticula are asymptomatic. Habein and associates[3] reported that in the 10-year period from 1944 through 1953 only 24 of 121 patients with proved pulsion diverticula underwent operation. Of the 97 remaining patients, most did not have sufficient symptoms to justify surgical treatment. Thirty-three patients had no symptoms whatsoever, and in only 17 were symptoms present which were caused by the diverticulum. In most of the other cases symptoms could be attributed to an associated hiatal hernia or esophageal spasm. Of the 24 patients who had operation, 17 had associated hiatal hernia, cardiospasm, diffuse spasm, or esophagitis; only 7 of the 24 did not have an associated lesion. A study of these cases would seem to indicate that unfavorable surgical results could be attributed to the presence of an associated disturbance of motility. Successful surgical treatment requires correction of this disturbance. In case 2 it is quite conceivable that a satisfactory result could have been obtained if myotomy and repair of the hernia only had been performed and the diverticulum had been left alone. In any case, we are of the opinion that every patient who is considered a possible candidate for resection of such a diverticulum should have the benefit of studies of esophageal motility.

Case 3.—A 41-year-old physician registered at the clinic on Oct. 22, 1956. He was primarily concerned with retrosternal pain which had occurred for the first time some 14 months prior to his registration. In all, he had had four or five episodes of upper substernal pain, most of which had occurred late in the evening when he was tired. On only one occasion had this discomfort been associated with exercise. In the three months prior to his registration he had noted some minor discomfort in the retrosternal region, with vague distress in the left arm. These attacks never lasted more than 10 or 12 seconds. Insufficiency of the coronary circulation had been suspected, but the clinical story had not been characteristic. Routine electrocardiographic studies had not indicated any abnormality, and electrocardiographic studies made in conjunction with exercise did not reveal findings which were diagnostic. Our examinations gave entirely negative results. Roentgenographic studies were made of the thorax, esophagus, and stomach, and evidence of abnormality was absent. Our electrocardiograms made after exercise showed minor changes which

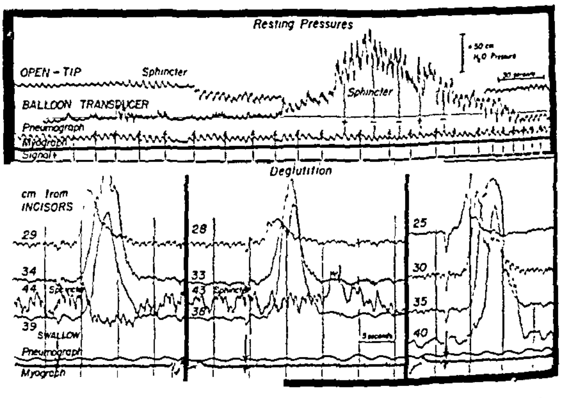

Fig. 5 (case 3).—Esophageal disorder mimicking angina pectoris; *top,* broad zone of excessive resting pressure in esophagogastric sphincter, with double reversal phenomenon. Tracing suggests small hiatal hernia. *Lower left,* tracing made in lower part of esophagus and sphincter after deglutition shows powerful simultaneous contraction characteristic of diffuse spasm. Sphincter relaxes at 44 cm. from upper incisor teeth. *Lower middle,* similar tracing, with distal unit at 43 cm. and no relaxation after swallowing. *Lower right,* midesophagus; contractions become peristaltic but are still too powerful.

could not be considered diagnostic of coronary disease. The patient was dismissed without a definite diagnosis and resumed his usual activities.

He returned to us on Jan. 12, 1959, complaining of symptoms similar to those previously described. He had continued to have episodes of substernal pain which occurred most frequently during the evening and which were sometimes referred to the upper thoracic portion of the spinal column, to the neck, or to the left arm. Again, after careful investigation, it was impossible to make a definite diagnosis of coronary insufficiency, and the possibility was considered that the pain might have an esophageal basis. Roentgenograms of the esophagus made on Jan. 16, 1959, did not show evidence of any abnormality. However, measurements of the esophageal pressures showed definite evidence of abnormal esophageal motility. Although peristaltic activity was evident after some swallows, many of of the contractions in the lower third of the esophagus were simultaneous, repetitive, and of excessive amplitude (fig. 5). The findings were characteristic of diffuse spasm of the lower part of the esophagus. The gastroesophageal sphincter relaxed normally after swallowing. A "double respiratory reversal" at the gastroesophageal junction was noted, which suggested the presence of a small esophageal hiatal hernia.

The evidence strongly suggested that the patient's pain was caused by diffuse spasm of the esophagus. A medical program was outlined, including elevation of the head of the bed and the routine use of antacids. The patient returned for further consideration on March 12 because of continued and persistent substernal distress of the type previously described. Roentgenographic study again gave negative results (fig. 6). The motility study was repeated on March 13 and the findings were similar to those at previous examinations although more advanced. The simultaneous contractions were of greater amplitude and duration than on Jan. 15, 1959. In addition, the gastroesophageal sphincter appeared to relax less adequately than at the time of the previous study (fig. 5) and it also contracted prematurely, suggesting that the sphincter now participated in the diffuse spastic disorder. The "double reversal" was still present. Further roentgenograms of the esophagus again failed to show evidence of any diagnostic signs. An esophagoscopic examination revealed slight evidence of thickening of the mucosa in the lower half of the esophagus, but little evidence of inflammatory reaction was noted.

A diagnosis of hiatal hernia could not be made by esophagoscopic means. Because of the fact that anxiety and tension seemed to play a major role in his problem it was felt that further observation should be continued. The possibility of a surgical approach in the form of a long myotomy was considered, however.

In this case, studies of esophageal motility clearly demonstrated that the patient's substernal pain was caused by abnormal contractions of the esophagus. Although a satisfactory solution to his problems had not been obtained, it was at least a source of great relief to the patient to know that he was not suffering from serious coronary insufficiency. In a number of similar cases we have been able to demonstrate an esophageal basis for thoracic pain which had previously been considered to be cardiac in nature.[4] Although the symptoms of diffuse spasm of the esophagus may be most unpleasant, they do not carry the serious prognosis implied by coronary insufficiency. The medical treatment of diffuse spasm of the esophagus is often unsatisfactory.

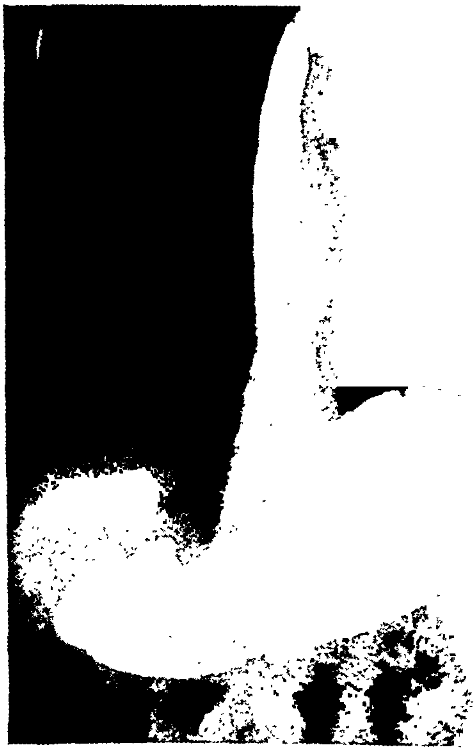

Fig. 6 (case 3).—Roentgenogram of esophagus and stomach, showing no evidence of abnormality.

Comment

Physiological measurements of pressure within the esophagus and at its sphincters have become an integral part of our examination in the diagnosis of nonstenosing esophageal disorders. A reclassification of esophageal disturbances based on physiological criteria is indicated. New entities in the field of esophageal disease continue to be described, and, on the basis of information obtained from studies of motility, our concepts of some disorders are being altered. These physiological measurements not only aid in the accurate diagnosis of esophageal disorders but also provide a more rational approach to the treatment of these conditions. In addition, studies of esophageal motility have proved to be of great value in the differential diagnosis of thoracic pain.

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REHABILITATION AND LONG-TERM SURVIVAL AFTER COLECTOMY FOR ULCERATIVE COLITIS

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and
Julius L. Berkley, M.D., Philadelphia

Colectomy was found necessary in 124 of a series of 468 patients with ulcerative colitis seen over 13 years. Fifty of the 124 patients had had colitis for five or more years. The resected part of the intestine contained a malignant neoplasm in 14 cases (11.3%). Five patients (4%) died postoperatively during their hospital stay, and six more (4.8%) died within 12 months after discharge from the hospital. Exclusion of the 14 patients with cancer left a total of 110 who were followed up for rehabilitation care; 50 of the 51 patients surviving 5 years and 19 of the 21 patients surviving 10 years were returned to an active, productive life.

In the annals of medicine there is perhaps no illness whose treatment has so completely defied all efforts at standardization as has that of nonspecific ulcerative colitis. It is indeed an outlaw among diseases. Its etiology has not been determined, its course is unpredictable, and its management is without established rule; yet through recent progress in medical science its ravages can be logically controlled. It is not uncommon to observe complete recovery and rehabilitation after surgical removal of the diseased intestine in patients with even the most advanced cases. When it is decided that colectomy is the indicated treatment in a particular instance, the patient, his family, and the referring physicians are entitled to know the facts about the mortality, the period of hospital confinement that might be expected, the chance of return hospitalization for correction of complications, the prospects of a resumption of former occupation and the relative degree of restraint imposed by that occupation, the prognosis of pregnancy, and the incidence of long-term survival.

The purpose of this presentation is to record our experience with a series of patients who have undergone colectomy for this disease. Unlike most reports, this discussion centers on postcolectomy patients rather than on clinical aspects.

Material for Study

In a personal series of 468 patients with ulcerative colitis there were 124 in whom colectomy was performed between September, 1945, and December, 1958, an incidence of 26.4%. All surgery was performed by one of us (H. E. B.). Of the 124 patients 54 were men and 70 were women; the youngest was 9 and the oldest was 76 years of age, the average being 37 years and 7 months.

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Associated Conditions.—In this group of 124 patients, various complicating factors resulting from the disease were encountered. Pseudopolyposis was demonstrated in 68 patients, an incidence of 54.8%; in 48 of the 68 the rectum was involved (70.5%). Of the 68 patients in whom pseudopolypoid change was found, carcinoma was present in 11, an incidence of 16.3%.

It is generally recognized that cancer of the large intestine is more common in patients with ulcerative colitis than it is in the general population, where its incidence was recorded as 0.02% by Svartz and Ernberg[1]; Counsell and Dukes[2] cited 11% associated with ulcerative colitis. According to Bargen and associates[3] cancer is 30 times more frequent in patients with ulcerative colitis. Kiefer and co-workers[4] reported cancer to be 66 times more common in a verified and 31 times more frequent in an unverified nonsurgical group. In our series of 124 patients undergoing colectomy, proved adenocarcinoma in the resected specimen was demonstrated in 14, an incidence of cancer of 11.3%. The average age in this group was 37 years and 7 months, which is in contrast to the average age of cancer patients in the general population, namely, 54 years and 5 months.

Of the 14 patients with cancer 8 (57.1%) were under 40 years of age. Nine are dead, one of whom lived five years and two months; five are living, two, four, five, and seven years, and four months, after colectomy.

It may be mentioned that, of our group of 124 patients undergoing colectomy, 50 had had colitis for five years or more, and of this number 13, or 26%, showed carcinoma of the intestine.

Anorectal Abscess and Fistula: It is understandable that infections in the anus and rectum would be encountered more frequently because of our type of practice. Of the 124 patients 54, or 43.5%, had, or had had one or more episodes of, anorectal abscess or fistula, or both. Five patients, or 4%, were found to have a fistulous tract between the colon and some other viscus or tegumentary surface. Ileitis, as disclosed by frozen section at the time of colectomy, was present in 51 cases, or 41.1%.

Mortality

In 124 patients five surgical deaths occurred during hospital confinement. Mortality according to the type of colectomy and number of stages of the operation is shown in table 1.

Intraoperative Mortality.—Two patients died within an hour after colectomy. In the first, a 52-year-old man, a one-stage ileocoloproctectomy was performed for severe ulcerative colitis. The second, a 40-year-old man, died after hemicolectomy on the right. He had undergone an ileostomy the previous year for severe colitis which was complicated by episodes of cardiac decompensation. His cardiologic diagnosis was hypertensive cardiovascular disease, with mitral regurgitation. Both patients had been under extensive steroid therapy. Autopsy performed in both failed to determine the cause of death, which was presumed to be due to steroid therapy. There were three post-operative deaths, on the 7th, 10th, and 11th days, respectively, from coronary occlusion; ileal dysfunction with peritonitis, atelectasis, and salt depletion crises; and peritonitis.

Death Subsequent to Hospital Discharge.—Death after discharge from hospital is more apt to occur during the ensuing 12-month period than later. Our cases are grouped as follows: (*a*) those for whom surgery was not instituted; (*b*) those in whom additional surgical intervention was required; and (*c*) those who died of associated intestinal cancer. All patients who died did so within the first year after colectomy except one who died seven years later.

TABLE 1.—*Mortality According to Type and Number of Stages of Colectomy*

Surgical Procedure	No. Stages	No. Cases Resected	No. Staged Resections	Deaths	Patient Mortality, %	Colectomy Mortality, %
Ileostomy, colectomy, proctectomy	1	48	48	2	4.1	4.1
Ileostomy and total colectomy, abdominoperineal excision	2	43* 41*	84	3	6.9	3.5
Ileostomy, total colectomy, abdominoperineal excision	3	9	9† 9 }18 9	...	...	...
Ileocolectomy with anastomosis	1	20	20	...	...	...
Left hemicolectomy	1	4	4	...	...	...
Total		124	174	5	4	2.8

* Patient did not return for proctectomy.
† Ileostomies not considered as resections.

Mortality in Patients with Fulminating or Toxic Ulcerative Colitis.—Although there are few reports of mortality in patients with the acute toxic or fulminating phase of the disease, it is well known that it is extremely high, irrespective of whether medical or surgical treatment is instituted. Bargen[5] was of the opinion that more patients will be saved by careful medical means than by surgical intervention. Crile and Thomas[6] reported that 36% of patients in this category died during the first hospital admission, regardless of the type of treatment. Furthermore, they found that after discharge from the hospital an additional 32% died, for a total of 68%. Follow-up investigation of their patients two to nine years after discharge revealed a mortality of 73% for those who had been under medical care and 63% for those treated surgically.

The term acute fulminating, or acute toxic, ulcerative colitis refers to a fulminant stage of the disease clinically manifested by intractable diarrhea associated with severe electrolyte-volumetric imbalance and systemic bacterial toxicity, reflected by temperature above 101 F (38.3 C), chills, and accelerated pulse, indicating an overwhelming process. It may become refractory to the most rigid emergency measures unless recognized before irreversible physiopathological changes develop.

Of our group of 124 patients undergoing colectomy, 23 were desperately ill. Each manifested considerable acceleration of the pulse rate, temperature of 101 F or above, and intractable diarrhea. Each patient was completely evaluated and prepared adequately for surgery over a period of from 10 days to three weeks, and in nearly every instance steroid therapy was instituted. These 23 patients fell into two categories, as shown in tables 2 and 3. In the first group (table 2), ileostomy with subtotal or total colectomy was performed in two stages; in the second group (table 3), a single-stage ileocoloproctectomy was used. In the 23 patients with acute toxic disease there was one death, for a mortality of 4.3%. Among the remaining 22 patients there were four deaths subsequent to hospital discharge. Thus 18, or 78.1%, are living and well three months to 10 years after total or subtotal colectomy performed in the presence of toxic ulcerative colitis, bearing out the importance of the most careful and precise cooperation between the gastroenterologist and the surgeon.

Table 2.—*Ileostomy and Subtotal or Total Colectomy With or Without Proctectomy in Patients with Toxic Ulcerative Colitis*

Age	Sex	Yr. of Operation	Status as of 1958
76	F	1953	Died later of inanition
26	F	1954	Living and well
45	M	1950	Living and well
40	M	1948	Living and well
35	F	1948	Died of intestinal obstruction, 1955
45	F	1956	Living and well
29	M	1956	Died in hospital, 1956
47	F	1956	Living and well
52	M	1956	Living and well
34	F	1958	Living and well
30	F	1958	Living and well
34	F	1958	Living and well
29	F	1958	Living and well

Table 3.—*Ileostomy, Total Colectomy, and Proctectomy in Patients with Toxic Ulcerative Colitis**

Age	Sex	Yr. of Operation	Status as of 1958
25	F	1955	Living and well
54	M	1955	Living and well
39	F	1953	Dead
37	M	1953	Dead
24	M	1955	Living and well
40	M	1956	Living and well
18	M	1956	Living and well
53	M	1956	Living and well
39	F	1956	Living and well
28	M	1957	Living and well

* There were no operative deaths.

Mortality from Complications and Sequelae Subsequent and Peculiar to Colectomy.—Of our total number of 124 colectomies 72 were performed in one stage, 43 in two stages (84 operations, since two patients did not return for proctectomy), and 9 in three stages (27 operations). Thus, 183 operations were required, according to the surgical procedure selected. In this group of 183 operations, 44 patients developed complications necessitating 56 surgical interventions, an incidence of 30.5%. Of the 56 operations 31, or 55.3%, were performed for revision of the ileostomy. It should be mentioned, however, that revision of the ileal stoma was required in only two instances, since we used the modified eversion technique. One patient was admitted on four occasions for ileostomy revision and another three times, including once for the removal of 240 cm. of ileum and jejunum. It will be noted that small-intestine obstruction, better termed ileal dysfunction in these cases, occurred in nine patients, with resulting death in three.

Impotence

Sexual impotence after coloproctectomy is a serious problem, particularly in young men. In a case in which the rectum is removed for malignancy the degree of radicality must of necessity be wide and extended, and injury to the sympathetic-parasympathetic innervation occurs frequently. The same is not true for ulcerative colitis, because the ileopelvic dissection is carried close to the intestine, thereby averting injury to the nerve supply. Our series includes 54 male patients; the rectum was removed in 47. If the two hospital deaths and the death after discharge, as well as the five in whom associated cancer was found, are deleted, there remain 39 male patients for evaluation. One patient in this group was impotent, which is computed as an incidence of 2.5%.

Period of Hospitalization

A decade ago it was the custom to use a three-stage operation, consisting of establishment of the ileostomy, removal of the colon, and, finally, removal of the rectum. It is understandable, therefore, that patients admitted to the hospital on three different occasions required more hospital days than those undergoing a two-stage procedure. In fact, little thought was given to the duration of confinement because of developing complications in many instances. Between the years 1950 and 1953 we held to a 21-day rule, in cases in which an ileal stoma was established, in order that patients could be fully instructed in its management; but over the past five years or so, our interest has become centered chiefly on the rationale of ileocoloproctectomy in which the entire surgical procedure is performed in a single stage. The refinements with the eversion technique of the ileostomy, and a better understanding of the physiopathology of ileal dysfunction, now enable us to discharge our patients on the 11th, 10th, or even 9th day after colectomy. Of the 48 patients undergoing a one-stage operation, the shortest period of hospitalization was 9 and the longest 67 days, the average being 17½ days. The patient having the longest stay had had 240 cm. of ileum and jejunum removed with the operative specimen.[7]

Fate of Patients After Colectomy

Pregnancy After Colectomy.—Inquiries about the possibility of pregnancy after colectomy and the effects, if any, on both mother and child, are not uncommon. According to the available reports it is the consensus that, in a woman whose rectum has been removed at the time of colectomy, subsequent pregnancy should be interrupted or delivery effected by cesarean section. The reason given is that the perineum is fixed and inelastic, rendering vaginal delivery dangerous, if not impossible. It is further believed that, in a case in which an ileostomy has been established, the enlarging uterus, especially during the second and third trimesters, may place abnormal stress and strain on the small intestine that is anchored to the abdominal wall at the site of the ileostomy. It has also been stated that, in cases in which the colon has been removed and an anastomosis established between the ileum and the rectum, cesarean section is the preferred procedure because small-intestine obstruction poses a continual threat until delivery is effected. We cannot agree with these opinions.

A review of our records discloses data of interest, even though the series is small. Twelve patients were delivered per vaginam, for a total of 17 gestations, with full-term deliveries. Five patients in whom colectomy with ileorectal anastomosis had been performed were delivered at term without complication to either the mother or the child, for a total of seven gestations. Our experience after ileostomy, total colectomy, and proctectomy includes 7 patients[8]; the youngest was 21 and the oldest 34 years of age. The ileum showed invasion by the ulcerative process in three and pseudopolyposis in four. The rectum and descending colon were involved in three and the rectum and the entire colon in four. The duration of the colitis ranged from three months to six years. The rectum had been removed as an integral part of the colectomy in all seven patients. There were 10 gestations in this group. In each instance, delivery was effected per vaginam, without use of forceps. No complications were encountered. All infants were normal at birth; one died subsequently of pneumonitis.

It is our considered opinion that pregnancy after colectomy can be managed effectively without fear of complications, although it is recognized that each patient should be individualized and guided through her pregnancy by the coordinated efforts of the obstetrician, the gastroenterologist, and the surgeon.

Fate of Remaining Rectal Segment After Colectomy for Ulcerative Colitis.—Inquiry is frequently made as to whether complications arise in cases in which the rectum is not removed as an integral part of the colectomy. Dennis and Karlson[10] reported a series of 41 patients in whom resection with ileoproctostomy was done with suture-line perforation and peritonitis in one, recurrent cancer and death in one, a new cancer in the rectum and death in one, recurrent severe proctitis and death in one, and recurrent proctitis and ileostomy in one. Our series embraces only 20 patients, but it should be stated emphatically that in not a single instance was the rectum preserved where there was or had been evidence of disease. For this reason, our results should be better than they would be had the rectum been the site of inflammatory change, stricture formation, abscess, fistula, or pseudopolyposis. Of our 20 patients, one for whom an ileostomy was established and the rectum removed developed a leak at the suture line. In another, extension to the rectum developed, requiring ileostomy and removal of the rectum. In one patient an ileostomy with colectomy was performed in 1949 as the first stage of the operation, but the patient did not return for the abdominoperineal removal of the rectum. Five years later the patient was admitted to a hospital outside of Philadelphia where an extensive rectal cancer was found. The patient died two months later.

It is our opinion that resection with ileoproctostomy may be chosen in the small percentage of patients in whom the disease is confined to the ascending, transverse, and upper descending colon and confirmed by accurate and repeated studies, and provided the rectum and sigmoid are and have been completely free of any disease.

Weight Gain After Colectomy.—Patients usually gain weight after colectomy, a gain that is particularly gratifying because appreciable amounts of weight have been lost in the course of their disease. Men especially are pleased, but, even though there is a coincident feeling of well-being and a remarkable mental adaptability, women are often reluctant to accept more than a slight gain. It may be recalled that Cave[9] reported an average gain of 45 lb. (20.5 kg.) in his 50 patients. A review of our records shows that, with the omission of the five postoperative deaths, the six who died within one year of their colectomy, the two who lived one year or less but then died of carcinomatosis, and one recently discharged from the hospital, 110 patients remain to be considered in the calculation. Five per cent gained no weight, 50% gained 21 to 40 lb. (9.6 to 18.2 kg.), and 1.3% gained 100 to 118 lb. (45.4 to 53.5 kg.), with an average weight gain of 29.4 lb. (13.6 kg.).

Long-Term Survival and Rehabilitation Incident to Colectomy.—It has been our custom, in calculating the 5-year and 10-year survival rates of patients with intestinal cancer, to delete the operative deaths, those lost to follow-up investigation, and those dying of diseases other than cancer. This method has been used by the British Ministry of Health since 1923 and more recently by the biometric division of the American College of Surgeons. However, for the sake of absolute fairness, our calculations of survival and rehabilitation are based on the 124 patients undergoing colectomy, with the exclusion only of 14 with cancer, even though of this number 2 are living and well after seven and five and one-half years, respectively, and a 3rd lived for five years and two months. No patients have been lost to follow-up investigation. Five, or 4%, died during their period of hospitalization, and six, or 4.8%, died in the ensuing 12-month period after discharge from hospital.

Therefore, 110 patients remain for calculation of survival and rehabilitation. There are 31 who are excluded because it is less than five years, at the time of writing, since they underwent colectomy. The rest, namely, 79, form the final group to be evaluated. Of these, 58 underwent colectomy prior to January, 1954, or more than five years ago. It is known that 51, or 87.3%, are alive and well five years or more after operation, of which number 50, of 98%, are completely rehabilitated. By the same token, 21 patients underwent colectomy prior to January, 1949, of whom 20, or 95.2%, remain alive and well 10 years after their colectomy. Of this number, 19, or 90.5%, are rehabilitated.

Summary and Conclusions

This study includes data on 468 patients with ulcerative colitis evaluated during a 13-year period, of which number 124 underwent colectomy, an incidence of 26.4%. The major associated complications of the disease included pseudopolyposis in 54.8%, anorectal abscess or fistula in 43.4%, ileitis in 41.4%, and intestinal carcinoma in 11.3%. In the group of those with carcinoma the average age was 37 years and 7 months, compared to the average age of all patients with cancer, 54 years and 5 months.

Five surgical deaths occurred during hospital stay, a mortality of 4%. There were 23 patients classified as having acute toxic or fulminating disease undergoing colectomy, with one death; 78.1% are alive and well three months to 10 years after colectomy.

It is our opinion that resection with ileoproctostomy should be reserved for the small group of patients in whom the disease is confined proximal to the descending colon, as confirmed by accurate and repeated studies, and provided the rectum and sigmoid are and have been completely free of disease. The long-term survival and rehabilitation rates in this series were 98% for 5 and 90.5% for 10 years.

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OVERCOMING THE DREAD OF FASTING.—Our present preoccupation with eating at regular intervals has led to the misconception that fasting is unpleasant. Possibly more attention to the Bible would have clarified the fact that fasting was not attended with discomfort but actually had beneficial effects. Scientific studies of fasting have extended the biblical observations and have shown that prolonged fasts are well tolerated. Fasting has been used to study metabolic changes since the very beginning of clinical investigation. Lucianni, Brugsch and Hirsch, Benedict and Grafe used this clinical technic for establishing many of the fundamentals of nitrogen balance, ketosis, water balance and metabolic rate. Pediatricians have in the past used this nutritional state in the treatment of epilepsy of children, and, from these studies, many basic concepts of electrolyte and water balance were elaborated by Gamble et al. Aside from the fundamentals elaborated by these earlier studies, certain unemphasized results of this preceding work have escaped attention. These observations are: Fasting is well tolerated for prolonged periods. After an initial short period, hunger is not a problem to the patient if he has free access to water. Vitamin deficiency does not occur in fasting. Weight loss exceeds that which would be expected from caloric expenditure of energy.—W. L. Bloom, Fasting as an Introduction to the Treatment of Obesity, *Metabolism,* May, 1959.

POSTOPERATIVE ENDOCARDITIS DUE TO PSEUDOMONAS AERUGINOSA

REPORT OF A CASE WITH RECOVERY

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Congenital cardiac anomalies, including a large interatrial septal defect, were repaired surgically in a 14-year-old girl. After an asymptomatic period of 20 weeks she began to have recurrent fever. Vigorous antibiotic treatment had only temporary effects. Reoperation showed that the original defects had been corrected but that one end of a silk suture was hanging free in the lumen of the right atrium and harboring Pseudomonas aeruginosa in pure culture. Removal of the suture was followed by uneventful recovery, ultimate resumption of full activity, and a satisfactory adolescence.

Prior to the antibiotic era, systemic infections due to Pseudomonas aeruginosa were rare. Now this organism, which is resistant to the usually employed antibiotics, is being reported more often as a pathogen.[1] Endocarditis due to Pseudomonas is fortunately still rare. A recent review [2] mentions 10 instances, all of which ended fatally. With the introduction of intracardiac surgery this ubiquitous organism has also found its way onto surgically acquired cardiac lesions.[3] The present communication reports a case which is of particular interest for several reasons. The possibility of an infection at the site of surgery was suspected early in the clinical course. There was relatively little evidence of renal damage from polymyxin B even though the patient received large doses of this drug intramuscularly for more than 100 days and intravenously for 10 days. Despite this intensive chemotherapy, results of blood cultures continued to be positive until a suture covered with an infected vegetation was surgically removed from the atrial wall.

Report of a Case

The patient was a 14-year-old girl admitted to the North Shore Hospital on March 22, 1957, because of unexplained fever of 10 days' duration. This was 20 weeks after intracardiac surgery had been performed.

She had been born prematurely, one of twins, weighing 4 lb. 10 oz. (2.1 kg.). In the neonatal period, heart murmurs were noted. Her early growth and development were essentially normal, but her school attendance was irregular because of frequent respiratory infections and fatigability. From 11 to 13 years of age her exercise tolerance diminished markedly and perioral cyanosis was often noted with her respiratory infections. Because of this, at 13½ years of age, she was referred to the Mayo Clinic for corrective surgery, with a presumptive diagnosis of interatrial septal defect and patent ductus arteriosus.

An operation, with the aid of extracorporeal circulation, was performed by Dr. John W. Kirklin on Oct. 25, 1956. At operation the significant findings were a wide short patent ductus arteriosus and a large interatrial septal defect. The ductus was about 5 mm. in length and 1.2 cm. in diameter at its narrowest portion. The septal defect measured about 3 cm. by 1.5 cm. in diameter. The ductus was divided and sutured with use of 00000 silk. The septal defect was repaired with interrupted 000 silk sutures supplemented with a continuous stitch. No other foreign materials were used. The postoperative course was uneventful, and the patient was discharged on the 14th postoperative day with marked improvement in exercise tolerance.[4]

The patient was completely asymptomatic until the 20th week postoperatively. At that time she began to have recurrent fever, to a temperature of 102 F (38.9 C), occasional pain over the lower part of the thorax, and anorexia. Penicillin and a tetracycline preparation were administered by her physician, Dr. John Gibbons, without effect. After 10 days she was referred to the North Shore Hospital.

Physical examination on admission revealed a thin, poorly developed 14-year-old girl who weighed 60.5 lb. (27.5 kg.) and was in no apparent distress. Her temperature was 99 F (37.2 C), pulse rate 90 per minute, and respiratory rate 24 per minute. Scars from a thoracotomy were present on the anterior chest wall. The heart was enlarged to percussion, with the point of maximal impulse in the sixth intercostal space about 2 cm. to the left of the midclavicular line. There was a regular sinus rhythm. The second pulmonic sound was markedly accentuated. A short grade 1 midsystolic murmur was heard along the left sternal border, mainly in the fourth interspace. The remainder of the physical

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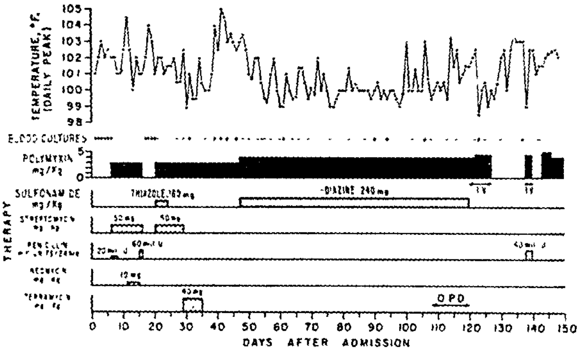
examination showed essentially normal results. Her hemoglobin level was 11.4 Gm. per 100 cc.; the leukocyte count 14,000 per cubic millimeter, with 74% polymorphonuclear leukocytes, 4% band forms, 20% lymphocytes, 1% monocytes, and 1% basophils. The sedimentation rate was 84 mm. per hour (Westergren). These hematological findings did not change appreciably throughout her North Shore Hospital stay.

The highlights of her subsequent hospital course are summarized in the figure. The first week was characterized by a fever curve with daily spikes of 102 to 103 F (38.9 to 39.4 C) associated with chills. The spleen became progressively enlarged until it could be palpated to the level of the umbilicus. Each of the six blood cultures drawn during the first six days grew a gram-negative rod identified as Ps. aeruginosa. Because of the history of congenital heart disease followed by recent cardiac surgery and because no other possible source of infection could be detected a diagnosis of endocarditis, probably at the suture site, due to Ps. aeruginosa was made.



Course of endocarditis due to Pseudomonas aeruginosa for first five months in a 14-year-old girl.

The patient was seen in consultation by Dr. Morton Bryer, and a course of therapy was planned. Therapy with polymyxin B (3 mg. per kilogram of body weight per day in four divided doses), streptomycin (50 mg. per kilogram of body weight per day) and penicillin (20 million units per day) was started while results of sensitivity studies were awaited. The polymyxin B and streptomycin were administered intramuscularly and the penicillin was given by intravenous drip. Serial dilution tube-sensitivity studies of this organism were made at the North Shore Hospital and in Dr. Bryer's laboratory at the Mount Sinai Hospital.

After two days, when the results of the sensitivity studies were known, penicillin therapy was discontinued. Two days later administration of neomycin (10 mg. per kilogram of body weight per day) was added. During the first day of polymyxin therapy the patient complained of circumoral paresthesia and generalized pruritus. These symptoms soon disappeared, with no change in therapy. However, from the fourth day of therapy on, marked anorexia, apathy, and vertigo were present. After the administration of neomycin was started, the anorexia increased and progressed until the patient refused all food and fluids by the 10th day of treatment. For this reason, and because three consecutive blood cultures taken during this period were sterile, it was decided to stop all antibiotic therapy. The next day the patient ate and took fluids well.

Thus, from her 17th to her 21st hospital day she was without specific therapy. Unfortunately, blood cultures on each of these days were later reported as positive for Ps. aeruginosa and the temperature curve, which had become lower, was again rising. Therefore, on the 21st hospital day, therapy was resumed with polymyxin B (3 mg. per kilogram of body weight per day in four divided doses) and streptomycin (50 mg. per kilogram of body weight per day); this time sulfathiazole (160 mg. per kilogram of body weight per day) was added. Results of blood cultures immediately became negative and the temperature curve became lower. Serial dilution tube-sensitivity studies were repeated on the organisms isolated on days 17 to 21 (see table).

On the basis of these new sensitivity studies, administration of streptomycin was discontinued on the 29th hospital day and oxytetracycline (Terramycin) (40 mg. per kilogram of body weight per day) and polymyxin B were given. The fever was soon better controlled, but one blood culture showed positive results for Pseudomonas. After six days of oxytetracycline therapy, the patient developed severe diarrhea. A pure culture of Candida albicans was grown from the stool and from the throat culture. Administration of oxytetracycline was therefore discontinued and nystatin was given to counteract the Candida infection. On days 35 to 47, polymyxin B was the only specific therapy used. During this period, neither the fever nor the bacteremia was controlled. On the 47th day, the patient experienced sudden severe pain in the left side of the chest. Roentgenographic findings compatible with pulmonary embolism were reported. Because of this, polymyxin B dosage was increased to 4 mg. per kilogram of body weight per day, and treatment with sulfadiazine (240 mg. per kilogram of body weight per day) was started. Therapy with both drugs was continued until the 120th day.

Under this regimen the bacteremia was again controlled and the fever slowly decreased. Up to the 90th day the bacteremia seemed to be fairly well controlled, with only 1 of 17 blood cultures growing Pseudomonas. The temperature, too, remained for the most part below 101 F (38.3 C). Clinically the patient appeared better. She was in good spirits, ate well, and gained some weight. Her spleen regressed in size until it was just palpable at the costal margin. After the 90th day therapy was temporarily discontinued. Recurrent bacteremia followed by a resumption of higher temperatures and by clinical deterioration then occurred. She had progressive anorexia and developed a *cafe au lait* skin color.

Within the first weeks of treatment, after blood levels of antibiotics had been achieved which were more than four times the in vitro bactericidal level, it had seemed that reoperation with the hope of surgically excising the focus might be necessary. Dr. Kirklin was consulted and urged to accept the patient. He was understandably reluctant to reoperate, and on the 120th day a trial of intravenous polymyxin B therapy was undertaken.[4A] Fifty milligrams of polymyxin (4 mg. per kilogram of body weight per day) dissolved in 250 cc. of 5% solution of glucose in water was administered over a 90-minute period every 12 hours. After two days this was increased to 60 mg. administered in the same fashion (4.8 mg. per kilogram of body weight per day). Intravenous therapy was discontinued after seven days, at which time the patient was afebrile and had negative results of blood cultures. On this day, albumin and white blood cells were noted in the urine in large quantity. No nitrogen retention or other signs of renal insufficiency were present. This evidence of renal irritation cleared even while the patient's condition was later being maintained with intramuscularly given polymyxin B.

Three days after discontinuation of therapy the patient became more febrile and results of blood cultures were again positive. Hence on the 138th day treatment with intravenously given polymyxin B (4.8 mg. per kilogram of body weight per day) was resumed and continued for three days. Intramuscularly administered polymyxin B therapy (4 mg. per kilogram of body weight per day) was then resumed. The patient became increasingly difficult to manage; she fought the repeated intramuscular injections, refused to eat, and became depressed. For this reason and because no more definitive medical treatment could be offered at this time, she was permitted to return home after her mother was instructed in the technique of administering polymyxin B intramuscularly. Meanwhile, further efforts were made to induce Dr. Kirklin to reoperate. On Aug. 16, 1957, he agreed, and arrangements were made to transfer the patient back to the Mayo Clinic.

On Oct. 31, 1957, an open-heart operation with use of hypothermia was performed. Dr. Kirklin stated that hypothermia was chosen because it was feared that the use of a bypass might cause widespread dissemination of infection due to the elimination of the filter provided by the lungs.

At operation he described a striking picture.

> The atrial septal defect repair was solid and well healed. There was, however, a silk suture about 2½ cm. in length dangling in the right atrium surrounded by fleshy material that subsequent cultures proved to be a pure culture of Pseudomonas organisms. This suture was removed and the atrium closed. . . . The pulmonary artery end of the ductus was visualized from within the pulmonary artery. This was entirely clean and there were no evidences of vegetation. A segmental resection of the anterior and medial basilar segments of the right lower lobe was done because of the lung abscess found to be in it.

The patient's convalescence from this operation was smooth and without incident. Three blood cultures taken postoperatively were all sterile. At the time of her discharge from the Mayo Clinic her appetite was good and she appeared improved.

At home the patient did well and soon resumed full activity. At the time of her second intracardiac operation, Oct. 31, 1957, she had weighed 48 lb. (21.8 kg.). When she was last seen at the North Shore Hospital on June 24, 1959, her weight had increased to 82 lb. (37.3 kg.). She had grown in stature and had matured sexually.

Comment

Preoperative Clinical Course.—The figure shows that 58 blood cultures were taken and that 21 of these were positive for Pseudomonas. Although chemotherapy did not cure the infection, it surely suppressed it. Thus, during 23 days before therapy and while therapy had been discontinued 13 cultures were taken and 11 (84%) were positive. During the 72 days while she was receiving at least 4 mg. per kilogram of body weight per day of polymyxin B plus sulfadiazine, 25 blood cultures were taken and only 4 (16%) were positive. During the 51 days while she was receiving polymyxin B, either alone or with some other chemotherapeutic agent, 20 cultures were taken and 6 (30%) were positive. Because of this suppressive effect and our inability to offer any more definitive medical treatment we were encouraged to continue with this unusually prolonged polymyxin B therapy at high dosage levels. The intravenously administered polymyxin B offered no advantages over the intramuscular route and appeared to increase toxicity.

Serial Dilution Tube-Sensitivity Studies on Pseudomonas Aeruginosa

	Before Therapy		After 10 Days' Therapy	
Antibiotic[*]	Bacteriostatic End-point, Mcg./Cc.	Bactericidal End-point, Mcg./Cc.	Bacteriostatic End-point, Mcg./Cc.	Bactericidal End-point, Mcg./Cc.
Polymyxin B	0.4	1	0.2	0.6
Streptomycin	1.0	4	[†]	...
Neomycin	1.6	4	7.5	[‡]
Oxytetracycline	1.0	...	1.0	...
Chloramphenicol	10	...	..	...

[*] Resistant to penicillin, 200 units/cc.
[†] Resistant to 25 mcg./cc.
[‡] None—Resistant to 25 mcg./cc.

Although the patient never developed petechiae, her spleen became larger when she appeared sicker and smaller as she seemed to temporarily improve. She had one definite pulmonary embolus and probably several smaller ones which we could not document. All this was consistent with vegetation on the right side of the heart.

During the entire course of therapy adequate urinary output was maintained and no signs of azotemia were present. Transitory albuminuria and pyuria occurred during the course of intravenously administered polymyxin B and continued for about two weeks after the cessation of this treatment; however, this cleared while she was receiving 4 mg. per kilogram of body weight of polymyxin B intramuscularly.

Source of Infection.—We do not know the source of this child's infection. It is of interest that Kerby[5] found 31.9% of 44 instances of Ps. aeruginosa infections to have occurred in the postoperative or postinstrumentation period. Of six reported cases of endocarditis due to Pseudomonas, three followed instrumentation or operation,[6] and one of these[3a] followed cardiac surgery. One of us (A. L. F.) with Schifrin[7] emphasized the ease with which instruments, particularly those not sterilized by heat, may become contaminated with Ps. aeruginosa. The original cardiac operation was performed on our patient with the aid of extracorporeal circulation with its multiple possible sources of contamination. This hazard is well recognized and means of overcoming it are constantly being sought. On this subject, Dr. Kirklin[4] wrote:

> This patient was operated upon during a period in which the mechanical pump oxygenator was sterilized by filling it with Zephiran. The Zephiran was thoroughly rinsed out of the equipment and the operation was performed. Because of the subsequent events in this case and because of several other similar cases the entire technique of sterilization of the mechanical heart-lung machine was altered in January, 1957. The use of Zephiran was abandoned and autoclaving of all parts except lucite reservoirs was accomplished. The lucite reservoirs were sterilized with the use of formaldehyde. Subsequent to the change in sterilization procedures there have been no further instances of bacterial infections.

It is by no means certain that the infection in our patient was acquired at the time of operation. In the case reported by Brundson and others[3a] of endocarditis due to Pseudomonas after mitral valvotomy, the infection was clinically manifest about seven days after operation. In our patient 20 weeks elapsed between the time of operation and the time of clinical illness. A sufficient number of cases has not been reported to enable us to predict the period of time which may elapse between infection and clinical illness.

Our patient was treated with penicillin for a long time preceding her first operation and during that postoperative period. McCurdy and Neter[8] pointed out that infection due to Pseudomonas organisms may complicate long-term antibiotic treatment, both with penicillin and with broad-spectrum antibiotics. The role of antibiotics in this case is difficult to evaluate.

Antibiotic Sensitivity.—As shown in the table, the organism on primary isolation was sensitive to polymyxin B, streptomycin, and neomycin. After only a short period of therapy with these drugs, resistance to streptomycin and neomycin appeared. The Pseudomonas organism remained, however, sensitive to polymyxin B even after prolonged therapy. This rapid development of resistance to streptomycin and neomycin is similar to the behavior in vitro[9] and illustrates the desirability of repeating sensitivity studies as often as is practicable during the course of an illness.

Limitation of Therapy with Polymyxin B.—Polymyxin B is an effective antibiotic when used against susceptible organisms and when these organisms can be reached by the antibiotic. Unfortunately, it is poorly diffusible. We were unable to sterilize a focus of infection on the endocardium, a region bathed by blood, even though we attained blood levels of more than four times that required for in vitro bactericidal effect. An obvious interfering factor was the probable thrombus-like vegetation. We were able to demonstrate in vitro that Ps. aeruginosa grown in a simple blood clot was not inhibited by any attainable concentration of polymyxin B, although in serum or saline suspension bactericidal levels of less than 1 mcg. per cc. were demonstrated. There are many differences between a simple blood clot and the vegetation of endocarditis, yet organisms harbored in the more complex vegetation are no doubt at least equally protected from the action of polymyxin B.

There is no doubt that only the surgical removal of the infected vegetation permitted the survival of this patient. Surgical treatment must now be seriously considered in endocarditis when intensive medical treatment fails. Prior to the availability of penicillin a successful surgical approach to bacterial endarteritis localized on a patent ductus arteriosus was reported by Touroff and Vesell.[10] The remarkable strides in chemotherapy made since that time have made such an approach necessary only infrequently. As in our case, however, when it is not possible to eradicate a focus with use of chemotherapy, surgery should be considered. With the recent advances in surgical technique for working on the heart, the risks attendant on such an approach are diminishing.

Summary

Symptoms and signs of endocarditis were noted in a 14-year-old girl about 20 weeks after an operation for correction of an interatrial septal defect and patent ductus arteriosus. The operation was performed with the aid of extracorporeal circulation. The patient subsequently developed endocarditis due to Pseudomonas aeruginosa. Polymyxin B given in large doses for more than 100 days—usually with other antibiotics or sulfonamides—failed to eradicate the infection. However, the combination of polymyxin B and sulfadiazine therapy seemed for a time to suppress it. The intravenous administration of polymyxin B offered no advantage over the intramuscular route and was more

toxic. Despite the long administration of polymyxin B (in doses of 4 mg. per kilogram of body weight) there was no permanent kidney damage.

Because of the failure of medical treatment, the suspicion that the infection was at the operative site, and the deterioration of the patient's condition, she was reoperated on by Dr. John Kirklin of the Mayo Clinic. He found a silk suture dangling in the right atrium surrounded by a vegetation which contained a pure culture of Pseudomonas. This was removed, as well as a portion of abscessed lung tissue. The patient's convalescence was uneventful. She was clinically well when last seen 20 months after operation.

As a result of this experience, and in light of the recent advances in cardiac surgery, it is suggested that when intensive medical treatment fails to cure bacterial endocarditis a surgical approach might be indicated.

Israel Rothenberg, M. A., offered technical assistance.

Burroughs, Wellcome & Co., through Dr. Erwin Whitman, supplied a portion of the polymyxin B used to treat the patient in this study.

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COOLING SUBJECTS WITH HYPERPYREXIA.—Hyperpyrexia and heat stroke are health hazards in a number of industrial occupations. No conclusive study has been published, however, to establish the best method of cooling men whose body temperatures are raised to hyperpyrexial levels. Consequently, some authorities strongly advocate cooling of such patients by means of ice-cold water; others are equally vehement that such a method is dangerous and not much more effective than cooling by means of evaporation of water from the body surface, aiding convection and evaporation by blowing air rapidly over the body. Some clarification of the problem was sought. . . . Six volunteers raised their rectal temperatures to 104 F by 40-50 minutes' work at 93 F wet-bulb temperature. The rates of fall in rectal temperatures were studied during cooling by six different methods. The most rapid method of cooling occurred when subjects sat at rest in an air condition of 90 F dry bulb and 87 F wet bulb and evaporative cooling was accelerated by wetting the body surface continuously for 1 hour; no significant difference in cooling was observed between airflows of 120 ft./min. and a jet of compressed air held 1-3 ft. from subjects. Merely seating individuals in air conditions of 70 F with 20% relative humidity in still air was almost as effective. Immersion in cold water and sitting in air conditions of 90 F (D.B.) and 87 F (W.B.) without aiding evaporative cooling are significantly less effective than the foregoing methods. . . . "Afterdrop" in rectal temperature after ice-cold water cooling may be associated with severe circulatory shock. Oral temperatures are a less reliable index of core temperature than rectal.—C. H. Myndham and others, Methods of Cooling Subjects with Hyperpyrexia, *Journal of Applied Physiology*, September, 1959.

CLINICAL NOTES

IRRADIATED BLOOD-TYPING SERUM

Robert M. Jamison, M.D., Denver

With the advent of nuclear weapons and warfare and the common use of radioactive materials the possibility of exposure of medical biological materials has become very real. This study was undertaken to determine what change, if any, occurs when blood-typing serum is exposed to ionizing radiation. With the threat of a nuclear war this problem should be anticipated and solved in advance.[1] A search of the literature does not reveal any previous studies on this problem.

Background

It is known that radiation will cause coagulation and precipitation of protein in solution due to a denaturing process.[2] The coagulation of proteins by radiation is irreversible. Changes in surface tension and viscosity of protein solutions have also been observed.[3] Similar effects in blood typing, which would result in alteration of specificity, might be anticipated.[4]

Materials and Methods

Blood-typing serum may be prepared in both wet and dry states. The typing ability of dry serum is not affected by indefinite storing, in contrast to that of wet serum.[5] The typing specificity of dry-typing blood serum appears to be as satisfactory as that of wet serum.

Pilot tubes were removed from blood bottles which had been typed and used for transfusions. The blood from the pilot tubes was retyped, with use of irradiated blood-typing serum, in both wet and dry states. Each specimen was retyped three times to check the consistency of the typing reaction. A control typing of each blood specimen was done in both wet and dry states, with use of fresh, nonirradiated blood-typing serum. The slides of typing serums were irradiated with a dose of 250 kvp. and 15 ma., at a target-slide distance of 50 cm. and a filtration of 0.5 mm. Cu and 1.0 mm. Al—equivalent to a half-volume layer of 1.5 mm. Cu. Slides prepared with dried typing serum were spread on a tray and irradiated. Approximately 50 slides were irradiated at the same time. The wet serum was irradiated in the serum bottles.

Each blood sample was typed as A, B, O, and Rh-positive or Rh-negative. The specificity and rapidity of the reactions was recorded. The radiation doses were increased in increments of 500 r in air until a total of 10,000 r in air was reached. Forty specimens were typed for each 500-r increment in dose. Dose levels higher than 10,000 r were not tested, since it is unlikely that exposures above this level would occur.

Results

Comparison of wet and dry typing serums irradiated at a dose level of 10,000 r with fresh, nonirradiated typing serum failed to reveal any change in the specificity of blood typing at the dose levels tested. Wet and dry typing serum irradiated to a total dose of 10,000 r in air, when compared with fresh, nonirradiated typing serum, showed no detectable alteration in the specificity of reaction. No delay was observed in the typing reaction. However, there did appear to be a slight acceleration in the rate of reaction of the Rh group with both wet and dry serums when the typing serums were exposed to 3,000 r.

Summary

Exposure of blood typing serums to a radiation dose of 250-KVP, up to a total dose of 10,000 r in air, resulted in no significant alteration in specificity of reaction in blood typing. They remained suitable for clinical blood typing.

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MEDICINE AT WORK

- *Families and Debts*
- *Survey on Stroke*
- *The Professions Join*
- *Rural America's Health*
- *100 Men for 14 Days*
- *Law and Medicine Mix*
- *System for Samples*

Sympathy That Hurts

What he calls the popular attitude of "Love that patient" in the treatment of the mentally ill is deplored by Dr. Sidney Bolter, a psychiatrist, in an article in the *Journal of Michigan State Medical Society* entitled "The Misuse of Sympathy."

Dr. Bolter says, "The person who uses sympathy as a tool, be he a physician or just a friend of the patient, is only reinforcing defect and calling attention to the patient's infantile desires and feelings. . . .

"The good psychiatrist devotes his attention, after a careful appraisal of the patient's strength and weaknesses, to getting the patient to study himself objectively, fairly and relentlessly, with the psychiatrist as a guide. This is not a pleasant task and is not one that involves sympathy. . . .

"In the case of many fringe practitioners of various mental disciplines, popularity comes from a technique which allows the patient to leave the office hearing exactly what he wanted to hear. . . .

"Sympathy is not a scientific instrument. It cannot be dispensed in any measurable amount, kill bacteria, remove or alter the function of diseased organs, immunize against ill health, and above all, it cannot foster psychological growth. . . ."

Committee members listen intently as a consultant discusses some of the problems involved in enforcing medical discipline.

Discipline and the Doctor—
The View from Atlanta

"Doctors are just ordinary people with special privileges. We've got to stop trying to prove that we are 100% pure."

This opinion was voiced by the executive officer of a state board of health at a meeting in Atlanta, Ga., last November when the A. M. A. Medical Disciplinary Committee met with physicians and officials of seven southern states in the second of its series of regional sounding-board sessions.

While there may be physicians still trying to prove that the profession is "100% pure," this attitude was not in evidence at the Atlanta meeting. The session was devoted instead to (1) examining the errors of that small percentage of doctors whose conduct is in need of control and (2) to a discussion of the ways and means through which such control can be effectively exercised.

As at the first regional meeting held in Denver last July, participants at Atlanta believed that both medical societies and state examining boards must bear down on errant physicians. Opinion was not nearly so unanimous, however, on just how this is to be accomplished.

The executive director of one state medical association was joined by several more in noting one of the chief difficulties. He said, "We have expelled doctors from our county and state medical societies only to find that, unless their licenses are revoked, these actions do not have much effect."

Agreement with this view was voiced by a member of the Committee, who pointed out that few, if any, patients recognize the importance of society membership. "To them," he said, "we're all doctors. I never yet had a patient ask me if I was a member of my county society."

Then what about state examining boards? Are they doing a proper job of policing their licensees?

"I don't see how they can," said the secretary of one state board, "since boards of examiners generally lack the funds to investigate complaints. One board, for instance, has an annual budget of only $6,000" But he agreed that discipline via examining boards ought to be promoted, because "the threat of license loss is potent, while loss of society membership may not be of such great concern."

Dr. Homer Pearson, secretary of the Florida board of medical examiners, and Chairman of the A. M. A. Judicial Council, agreed that funds are not sufficient to allow such boards to investigate complaints. He said, "In Florida, we plan to ask the legislature to assess each licensee $10 annually, with the money to be used for disciplinary purposes." Under the Florida plan, he said, the board of examiners would have the funds they need.

The secretary of another state medical association pinpointed a legal concern that sometimes operates to protect medical wrongdoers from the consequences of their actions. He noted that in many states accusing physicians refrain from filing complaints because of the fear of being sued. But to Mr. C. Joseph Stetler, Director of the A. M. A. Law Division, this aspect of the problem is not so serious as it has been pictured. He said, "The possibility of legal repercussion has been greatly overplayed. If the cause for the disciplinary procedure is valid, this is the easiest kind of case to defend, if it is properly handled."

Asked to enumerate the problems current in their states, the doctors displayed a marked similarity in presentation. Their chief concerns are with physicians who abuse the benefits of health insurance, who drink to excess, who use narcotics, and who are mentally ill. In discussing remedies for these and other disciplinary situations, the Chairman of the Committee, Dr. Raymond McKeown, warned that offenses must be properly segregated to be successfully disciplined. "We must define the difference between medical society discipline and board of examiners discipline," he said. He noted that it is possible for an action to be unethical but perfectly legal.

The crux of medicine's disciplinary problems, as they were viewed in Atlanta, seemed to be summed up in two statements made at the meeting. One physician said, "Every state medical society suffers from timidity in matters of discipline. We've got to get more hardboiled." And another queried, "Why ask the legislatures for more law when we don't use what we've got?"

Dr. Raymond M. McKeown of Coos Bay, Ore., is Chairman of the A. M. A. Medical Disciplinary Committee. Other members are Drs. James H. Berge of Seattle; Paul G. Henley of El Dorado, Ark.; H. Thomas McGuire of New Castle, Del.; and E. G. Shelley of North East, Pa. Consultants are Drs. Stiles D. Ezell of Albany, N. Y., and Harold E. Jervey of Columbia, S. C. Staff Secretary is Mr. C. Joseph Stetler of Chicago.

Impartial Medical Testimony Is Spreading—But Watch Out

With three out of every four cases on our nation's crowded court calendars requiring some type of medical report, is justice best served by one physician, testifying as an "impartial expert," or by two or more doctors presenting differing viewpoints? Like many another question in medical jurisprudence, it is difficult to answer, for there are pros and cons in both arrangements (see Medicine at Work, The Journal, *April 25). For example, an "expert" cloaked in medical-judicial authority might tend to take advantage of the inexactness of medical science—while the "conflicting" testimony of physicians in our traditional adversary system of legal proceedings can further delay a case already held up in court log jams. Currently, the "expert" system is growing:*

For the first time, a national medical organization has come out in favor of plans in which authoritative medical and judicial bodies agree jointly to cooperate in securing the testimony of impartial medical experts. In an October resolution addressed to the A. M. A., the American Association for the Surgery of Trauma recommended that the establishment of such plans "in appropriate areas be encouraged by all possible assistance and advice."

This move is being watched closely by the A. M. A. Law Division, whose director, C. Joseph Stetler, said last August at a meeting of the American Bar Association, "I personally would hate to see impartial medical testimony projects seized upon by physicians as an avenue of escape from their responsibilities as medical witnesses. . . . While medicine does not feel that a panacea has yet been discovered, however, it does look with interest on such projects and considers them a constructive approach."

Variations of the impartial medical testimony plan appear to be gaining adherents. According to the A. A. S. T., in nine states—California, Illinois, New Jersey, Maryland, Massachusetts, Minnesota, Ohio, Pennsylvania, and New York—such plans either have been instituted or are being considered as a means of clearing away mountains of personal injury claims. In the past year alone, impartial medical testimony plans have been discussed at more than a dozen big-city meetings of medical societies, judicial groups, bar associations, and other organizations.

The plan's greatest success, undeniably, is being chalked up in its birthplace, New York City. There, where it has been in operation for seven years, recent figures indicate that questionable claims are dwindling and fewer cases are coming to trial. Why? Advocates of the system say it is because lawyers have recognized the proficiency of the physician panel on matters of a medical nature.

Stroke Rehabilitation— Georgia Checks Its Status

The Situation: There are six senior medical students, supported by fellowships, available for an eight-week summer project.

The Problem: Which of the dozens of worthwhile studies they might make will prove the most valuable?

This is the decision that has been made annually since 1956 by the professional education committee of the Georgia Heart Association. Past studies have been in the fields of rheumatic fever prevention, reemployment of cardiac patients, and a case register of patients with rheumatic fever. Last summer, GHA's cardiac rehabilitation committee requested that the students poll as many as possible of Georgia's 3,320 physicians on their experiences in the rehabilitation of patients who had suffered from stroke.

Mr. M. Linwood Beck, executive director of the GHA, explains the decision this way: "[The committee] suspected that the average stroke patient receives good care in the early stages but that, for any number of reasons, rehabilitation procedures are not continued after he reaches home. This led to the conclusion that something should be done which would enable the families of stroke patients to carry out proper rehabilitation in the home."

Although the committee had ideas of its own on how to proceed, it felt that the development of an adequate program would depend on the experiences of physicians in their own practices, the extent of their interest in such a program, and other factors which could only be answered by the physicians themselves. So, the decision was made to survey Georgia's doctors.

After the Fellows were chosen and the survey procedure outlined, the six candidates—five men and a woman—were put through a week of orientation not only on the clinical and psychological aspects of stroke but on survey techniques as well. In addition, each student made several "dry runs" on physicians who were expecting them and who were asked to check on their survey techniques.

Thus armed, the six split the state's 159 counties among them and set off. The students' impending arrival in each office was announced beforehand by a card mailed to those physicians to be visited in the following week. Once in the physicians' office, the student asked a series of questions on the number and types of stroke cases encountered and the forms of therapy, management, and rehabilitative technique and assistance.

Mr. Beck emphasizes that "The objective of this study is to [gain] an insight into the problems, the attitudes and the reactions of physicians to certain cardiovascular problems in which the Heart Association is interested. It serves as an excellent guide to our professional education committee in planning its activities and points of emphasis, because it provides a good index to both the weaknesses and strengths of medical practice in Georgia."

Waiting Room Woes

The comments of the medical students making the rounds in Georgia's stroke rehabilitation survey provide some amusing sidelights on the life of a medical pollster.

One said, "The average waiting time in each office was approximately 40 minutes, with extremes varying from 10 minutes to three hours. The majority of the doctors were reached on the first visit, but a moderate minority required from two to four visits. As it became necessary to visit an office more than two times, it became less likely to see the doctor because of the receptionist's unwillingness to cooperate. She seemed to acquire an unusual glibness in making excuses for not announcing you."

The students interviewed 1,200 doctors in the course of the summer and learned a good deal about medical practice in the bargain. Said one student (male), "One qualification for an interviewer is to be able to get in to see the doctor easily. A female is much more welcome." Said another interviewer (female), "But of course the key to the doctor's office is his receptionist—invariably a female—unfortunately."

The Growing Challenge Of Disability Control

The trend is described this way: The total medical dollar is buying less and less while the public is demanding more and more comprehensive health care. This is the problem: How, in the light of such a trend, can extended disability be controlled, particularly those afflictions which account for most of the disabled?

The problem was tackled last month in Boston at a symposium featuring leaders in the medical profession and allied fields, the insurance industry, law, labor, and government. Dr. Gunnar Gundersen, immediate past-president of the A. M. A., said at the symposium, sponsored by the Liberty Mutual Insurance Company, on Oct. 16, "The physician's responsibility takes many new turns, such as directing a patient to additional facilities which can provide the care he needs; awareness of importance of rehabilitation to the patient and to society; cooperation with company health and welfare activities; maintaining a pattern of practice which starts with preventive medicine and ends with rehabilitation."

The Boston conference explored two phases of the disability control problem—the latest research findings on degenerative disease and cardiac disability, and the psychological conditions which impede recovery, and the medical economic pressures which are intertwined. In assessing the symposium, the secretary of its advisory committee, Edward T. Chase, said, "Social groups are registering impatience with the traditional institutions in the health care field, are in some cases invoking the assistance of the federal government, and are striving to bring about basic improvements in our health care system. Medicine is rising to this challenge by new techniques and by embracing a more comprehensive philosophy of medical care, stressing preventive and restorative as well as curative aspects."

Wife, Children, and Debts Often Precede M.D. Degree

The person who gets an M.D. in the United States today is likely already to have acquired a wife, children, and debts.

The last annual report of the A. M. A. Council on Medical Education and Hospitals (The Journal, Nov. 14, 1959, page 1507) indicated that of 100 typical graduates 62 were married, 30 had one or two children, 4 had three or four children, and 52 were in debt, 17 of them over $5,000 and 6 of them over $10,000. The 6,860 graduates had a median age of 26.

Enrollment in the 85 approved medical schools in the nation reached a record 29,614. Single students spent an average of $2,400 a year and married students with three children $3,900. Only 5 of the schools had rental living quarters for all students but 35 had them for part of the student body. Rent for single men varied from $140 to $840 annually and for married students from $171 to $1,050. Of the first-year studies, 27% were married.

Despite family and financial obligations, approximately 9 out of 10 students entering medical school graduate. Of the 1,012 dismissals or withdrawals, 90% were of first-year or second-year students and 60% were for low grades. Nonacademic reasons were given for the departure of the other 421 students, of whom 79 were in their third and fourth years of school. The Council is trying to determine whether lack of money is a major reason why upperclassmen are lost to medicine.

The nation's medical schools had 8,128 first-year students, representing 54% of the persons applying for admission (in contrast to 28% 10 years ago). The average student applied to four different schools in the hope of being accepted by one.

Statistics show a trend toward longer premedical training. Eighty per cent of the students had had four or more years of college and 20% had three. One can still start medical school with less than three years of college, but in the entire United States, last year, there were only five students who did.

Focusing a Mirror on The Medical School Complex

The medical school is not just a building. It is at once a mirror of the public's health, a complex of broad economic problems, and a focal point for progress in many sciences. Those characteristics were brought out by at least 4 of the 35 speakers before an Association of American Medical Colleges meeting early last month. Nearly 1,200 physicians and others interested in medical education assembled in Chicago for the AAMC's 70th annual session. They heard Surgeon General Leroy E. Burney of the Public Health Service say:

"The intelligent layman may be aware that the expense of a lengthy medical education today is almost prohibitive, but he may still have reservations about urging a special scholarship program for a particular group of students whom he views as preparing for a high-income career. . . . The problems of medical education are too large, too fraught with vital import, to be brought anywhere near solution unless they are recognized and dealt with as matters of public policy by responsible leaders at all levels of government and in all sectors of national life."

In fact, said Eugene N. Beesley, president of Eli Lilly and Company, the whole subject of medical care has become almost as much of an issue with the public as social security and full employment were during the 1930's. But, he added, "Medicine in a changing world is marked by accomplishments in furthering human health which were beyond our fondest dreams only a few short decades ago. These are not the contributions of a lone scientist working in a basement laboratory but result from the brain power and energies of many."

Progress was cited by another conference speaker, Dr. Max Michael Jr. of the University of Florida school of medicine, who revealed that a television circuit which will link six affiliated hospitals with the university is now in the active planning stage. (See Medicine at Work, The Journal, March 21.) He said, "The ability to televise conferences among hospitals will be economical of time for both house staff and attending staff."

No matter how scientific knowledge is communicated, however, it must be approached on the level of human understanding, according to Dr. Paul J. Sanazaro of the University of California school of medicine. He said, "In the context of medical teaching, teacher and student are exact counterparts of the physician-patient relationship. As we strive to teach students to deal with the 'whole patient,' should we not deal with the 'whole student?'"

Life Underground Charms Prisoners out of Their Cells

Except for the time of year, it looked like a ritual celebration of Ground-hog Day last month as 96 men emerged from their underground burrow, blinked at leaden skies, and decided to stay above ground.

The 96 were what remained of the 100-man complement that went underground 14 days earlier at Parks Air Force Base in California in a fall-out shelter test sponsored by the Office of Civil and Defense Mobilization (see Medicine at Work, The Journal, Oct. 10, 1959). Except for a handful of scientists from the Naval Radiological Defense Laboratory in San Francisco, the shelterites were prisoners from one of California's model penal institutions, the Santa Rita Rehabilitation Center. All had volunteered to undergo the two-week test in the 25-by-48-ft. structure, described by Mr. Walmer Strope, shelter commander, as a "sort of underground Quonset hut." The structure is produced commercially and is of a type used by the Navy for ammunition storage.

Purpose of the test was to check on the physiological, psychological, and sociological behavior of a large group forced by circumstance to go underground in crowded and uncomfortable conditions. Three Navy physicians—Capt. Harry Etter, Lt. David Katz, and Lt. Leonard Taylor—kept a constant medical check on the men's conditions. None of the three stayed for the entire period; instead they shared the duty in several-day shifts.

Prior to their selection as participants in the test, all volunteers had to undergo both physical and mental exams. Such screening may have paid off, because there were few arguments, and no fights, in the shelter.

The structure was equipped with a 6-by-2-ft. bunk for each man. Occupants slept head to toe to cut down on respiratory infection. The bunks were folded up during the "day," and such games as shuffleboard provided a mild form of exercise. There were checkers, cards, and books for entertainment, but the men complained of boredom as well as their diet and the isolation. They underwent an average weight loss of 5 lb. (2.3 kg.) per man.

Measuring the success of the test will not depend on the subjective reactions of the volunteers alone. A 24-hour-a-day instrument check was made on the physical conditions inside the shelter, which is equipped with air filters and ventilators as well as electrical and sanitation systems.

The project's backers call the trial an "unqualified success" but admit that a rougher test will come when women and children are added to the shelter's complement, a test planned for next year.

Of the four men who failed to stay down for the full two-week period, two had to be evacuated for medical conditions. The other two had a more esoteric reason: they were due in court.

The Sheltered Life

While volunteers stayed underground in California to prove that shelter life is possible, both the federal government and private persons sought to prove elsewhere that living in a shelter can be comfortable as well.

In Washington, the Commerce Department built a full-sized family shelter on its front sidewalk and equipped it with food, water, beds, a ventilating device, and a tape-recorded spiel to attract passers-by.

In Chicago, a past-president of the American Institute of Decorators designed and built a shelter called "The Family Room of Tomorrow." On display in the lobby of the city's Merchandise Mart, the model sported such attractions as a hopscotch court inlaid in the vinyl flooring and a stationary bicycle that provides exercise and pumps air at the same time.

Delaware Doctors Tune In On Postgraduate Education

A feeling of medical "togetherness" is not always easily come by. However, such a feeling is a by-product of an easily available postgraduate educational opportunity offered by the Medical Society of Delaware in a series of lectures via FM radio (see Medicine at Work, The Journal, March 21, 1959).

The lecture-and-question programming is done through the facilities of WHYY, an educational station in Philadelphia. Topics for the broadcasts are chosen by a poll of all Diamond State physicians. Programs are then broadcast at specified times, and physician groups meet in seminar fashion at all of Delaware's general hospitals.

Although many such groups convene, only four have the facilities for two-way radio communication with the home station that allows the doctor to question the lecturer. Such questions are written out and handed to the group's moderator. The moderator is the only physician actually heard on the air during the question period.

Most seminars are held in hospitals, but in Dover a room is reserved at a local hotel and in Wilmington the group meets at the Delaware Academy of Medicine. The programs were initiated by the state society's committee on education and are co-sponsored by a pharmaceutical firm.

A Delaware doctor with a question that doesn't get answered during the allotted time period needn't feel deprived; enrollment in the course entitles him to an answer by mail.

Drug Sample Discards—Gifts for Medical Missions

What happens to professional drug samples offered to the doctor? What fate awaits the packaged potions dropped by letter carrier or detail man on the receptionist's desk? Pharmaceutical advertising directors hope such samples will be used, by either the physician or his patients. The sad fact is, however, that many samples are discarded.

To divert such discards to useful channels is a project recently undertaken by the men's group of the St. John's Presbyterian Church in Miami, Fla. With the blessing of the Dade County Medical Association, the churchmen are mounting a drive to collect unused drug samples from the county's physicians for relay to medical missions overseas. Sorting and packing are to be performed by professional help, and no narcotics will be included, according to Mr. R. H. Johnson, vice-president of the church and director of the project.

A similar effort was completed in Chicago recently by Gloria Kelson, R.N., coordinator of patient-nurse relations at the University of Illinois Hospital. Learning that a Methodist mission hospital in the Belgian Congo was short of medical supplies, Miss Kelson collected more than 1,000 drug samples and shipped them off to Africa.

Charitable uses for castoff samples are not unusual. A survey conducted two years ago by a marketing research firm showed that almost 10% of the samples reaching the surveyed physicians were sent to either charity patients, missions, or hospitals.

But there's still room for other projects of the Dade County and Chicago types. The survey also estimated that "almost a third of all samples are really wasted—hit the wastebasket, go down the drain, or are burned."

Health in Rural America—A Preview of Grand Rapids

What sort of health problems face the nation's farm people? The same kind that face the rest of America, with a few added ones for good measure.

This fact is illustrated in the planning for the 15th National Conference on Rural Health to be sponsored February 25 to 27 at Grand Rapids, Mich., by the A. M. A. Council on Rural Health. Such program topics as careers in the field of medicine, aging, and immunization might be found on any health conference agenda, but such concerns as the feeding of hormones to livestock and the health programs of 4-H clubs are imprinted with the characteristic stamp of rural America.

These subjects—and many more—occupied members of the Council when it met last fall in Chicago to plan the Michigan conference. On deck to assist in the project was the Council's 14-man advisory committee, made up of representatives of agricultural organizations, farm publications, and educational groups.

"Meeting Challenges With Responsibility" is the theme of the conference, which may attract as many as 600 physicians, nurses, dentists, youth leaders, and farm group representatives, if it follows the examples set by such affairs in the past. Included in the Grand Rapids program are:

—A panel presentation on careers in the field of medicine which will include as participants advanced medical and dental students, a student nurse, and a laboratory technician.

—A discussion of aging with a Meet the Press format, in which both physicians and laymen will be quizzed on the outlook for America's elderly.

—A session dealing with such nutritional topics as foods, additives, and faddism.

The conference's final session on Saturday morning will emphasize the need for immunization. Aside from the subject's intrinsic importance, the session will have an even greater meaning: it has been chosen to mark the kickoff of a year-long immunization campaign to be waged by the Council and its advisory farm organizations in 1960.

Directorate

The Council on Rural Health differs in one organizational respect from most other A. M. A. groups of a similar nature; it has a group of regional directors.

Four newcomers to the Council have recently accepted responsibility for the following states:

Dr. Herbert E. Mason of Beaverton, Ore.—Idaho, Washington, and Oregon.

Dr. Samuel Leinbach of Belmond, Iowa—North Dakota, South Dakota, Iowa, Nebraska, Wisconsin, and Minnesota.

Dr. Reed W. Farnsworth of Cedar City, Utah—New Mexico, Colorado, Utah, Montana, and Wyoming.

Dr. Edmond K. Yantes of Wilmington, Ohio—Michigan, Missouri, Ohio, Indiana, and Illinois.

Directors of the other regions are Drs. Norman H. Gardner of East Hampton, Conn.; Allen T. Stewart of Lubbock, Texas; W. Wyan Washburn of Boiling Springs, N. C.; Charles R. Henry of Little Rock, Ark.; and Carroll B. Andrews of Sonoma, Calif.

Members of the Council's Executive Committee include Drs. Fred A. Humphrey, Chairman, Fort Collins, Colo.; Carll S. Mundy, Toledo, Ohio; and Dr. Gardner, Vice-chairmen. Dr. F. S. Crockett of West Lafayette, Ind., is Chairman emeritus.

Session in Chicago

Insurance for Mental Illness And General Hospital Care

Should voluntary health insurance programs be enlarged to cover mental illness? Should more mental patients be treated in a general hospital near home, rather than a huge state institution far away?

Strong encouragement for both these trends was heard from many of the 175 participants in the Sixth Annual Conference of Mental Health Representatives of State Medical Associations at the meeting in Chicago, Nov. 20-21, 1959, sponsored by the A. M. A. Council on Mental Health.

Persons attending included superintendents of state and private hospitals, psychiatrists in private practice, representatives of state societies, and other workers in the field of mental health. They exchanged ideas informally by splitting into six discussion groups. The following extracts are selected from the summaries prepared by official recorder-reporters for the panels:

On Mental Health Insurance.—Every effort should be made to obtain coverage for mental patients equal to that provided for medical and surgical patients. Despite recent growth of this type of insurance, psychiatric patients in many localities do not receive the same full benefits. . . . Some plans exclude all psychiatric illness, others give only minimal coverage.

On Oversized Institutions.—We are distressed at the bigness of mental hospitals. We wish them small. They are located at [great] distances from the community they serve. Facilities are inadequate and arranged for mass care. Today we would have small groups and encourage social interaction. . . . We urge that not another building be erected to add more beds to a large public mental hospital. All new construction should be to provide community mental health centers and general hospital facilities for psychiatric patients.

On More Open Treatment.—There cannot be any healthy attitude toward the mental patient when hospitals are cloistered and psychiatrists difficult to communicate with. Past tendency has been to shroud mental illness in an aura of mysticism. There has not been good communication between the psychiatrist, general practitioner, and . . . family. . . . There is little question that the open hospital is one of the answers to the antiquated stigma of mental illness. The trend to remove excessive, obtrusive, and anxiety-provoking features whenever possible was approved. Resulting improvement in therapeutic atmosphere far outweighs potential hazards. . . . Presence of a psychiatric unit in a general hospital fulfills many functions. The whole hospital becomes a better hospital as a result of its influence. It reduces the distance which still exists in many quarters between psychiatry and other medical specialties, gives a golden opportunity for psychiatrists and nonpsychiatrists to meet, [and] acts as a leavening influence by introducing principles of modern psychiatry into every aspect of the general hospital.

On Changes in Commitment.—Use of policemen and jails in commitment of mentally ill patients was disapproved. If state law prohibited jail use other facilities soon would become available. Commitment for an indefinite period is preferable to one for a specific time. State laws should permit voluntary commitments. . . . Legal proceedings should distinguish between committing a patient and declaring him incompetent. There is no reason why every person committed should automatically be considered incompetent.

On Release and After-care.—Better methods are needed for discharging patients able to get along on convalescent care outside the mental hospital. Good medicine dictates that concrete recommendations be made for the patient to remain in touch with his local physician or after-care clinic. The best tool for implementing the rehabilitation program is the general practitioner. There still is a great lack of psychiatric education in medical schools. In many areas follow-up care is meager or unavailable.

On Role of Private Hospitals.—Private psychiatric hospitals have 2% of the psychiatric beds in the United States, yet receive some 40% of all relatively acute, potentially recoverable [patients on their] first admissions. Physicians are asking more and more that staffs of these hospitals supply public education to the community.

On Rural Limitations.—In certain rural areas, psychiatric facilities are limited. Psychiatrists can establish better community relations, train their own psychiatric personnel, and encourage physicians and nurses to settle there. . . . In one state, two psychiatrists, working with the American Academy of General Practice, presented three-day programs to help other physicians understand when to care for psychiatric patients themselves and when to refer them for specialized treatment.

On Medicine's Duty.—Organized medicine has an obligation to support budgetary and legislative action for better care of the mentally ill. Medicine at large has defaulted in its obligation to the general public in extending the notion that the indigent medical or surgical patient is worth a greater expenditure of money than the indigent mental patient. This concept is untrue.

Dr. Leo H. Bartemeier of Baltimore is Chairman of the A. M. A. Council on Mental Health. Other members are Drs. Walter H. Baer of Peoria, Ill.; Norman Q. Brill of Los Angeles; Hugh T. Carmichael of Chicago; Hamilton F. Ford of Galveston, Texas; Francis M. Forster of Madison, Wis.; George E. Gardner of Boston; M. Ralph Kaufman of New York; and Lauren H. Smith of Philadelphia. Dr. Richard J. Plunkett of Chicago is Staff Secretary.

Anniversary in Michigan—Toward Unity in the Professions

Many of the problems, aims, and triumphs of medicine share common ground with those of other professions. Created in that concept, the Michigan Association of the Professions this month observes its first anniversary. Next month, on Jan. 22 and 23 in Detroit, the 2,500-member organization will take another step forward when it convenes its first Congress of the Professions.

It was in 1957 that the house of delegates of the Michigan State Medical Society endorsed the idea of its president, Dr. George W. Slagel, that all professions might work together for the mutual benefit of the professions and the people they serve. Last year, medical leaders met with boards of the Michigan Society of Architects, State Bar of Michigan, Michigan Society of Professional Engineers, and Michigan State Dental Society—and on Dec. 1, 1958, MAP was born as a nonprofit corporation inviting other professional groups to join in its program.

Since then, according to the president of MAP, William M. LeFevre, M.D., of Muskegon, inquiries aimed at forming similar state organizations as well as a national association have been received from more than a dozen states. As a consequence, MAP is now preparing an administrative pattern for possible use outside of Michigan. After one year of operation, the organization believes it has made promising strides along legislative, public relations, business, and educational lines. These include review of state tax proposals affecting the professions in Michigan, taped radio programs describing the role of professions in our society, various group fund programs for members, and endorsement (in principle) of a $1,000,000 educational fund for scholarships to students considering professional careers.

In what settings can the professions work more closely together in day-to-day activities? MAP cites these examples: medical testimony in court; the common interest of physicians and dentists in oral surgery; the close relationship between architects and engineers; and the joint efforts of doctors and engineers to improve occupational health. Dr. LeFevre cites another advantage in interprofessional unity:

"Industry and labor each are represented at the bargaining and legislative tables of the nation by a single, powerful voice. Legislators consult—and listen to—their wishes and demands. On the other hand, the professions are rarely considered, much less consulted, except in those rare instances when the matter directly affects one particular profession. It is ironic that at a time when the nation is crying for brainpower the professions, the most learned group of all, are being bypassed when decisions affecting their future are being made."

A University Serves

Doctors Teach Police and A Campus Houses a Coroner

Training a police officer is not generally thought of as a doctor's duty, nor is helping a university function one of the traditional roles of a county coroner. But in greater Cleveland both of these practices have been in effect for seven years, ever since the founding of the Law-Medicine Center at Western Reserve University. The center, established to bring a closer liaison between two ancient professions, has developed some unusual, and perhaps unique, features.

An $800,000 laboratory and office building of the Cuyahoga County coroner is part of the center, along with the school of law, the school of medicine, and the institute of pathology. All of them stand close together on one section of the campus.

Since its beginning, the center has divided its instructional activity into two phases of justice—civil and criminal. As part of the latter, a school for suburban police officers was established.

Four-Man Administration

Director of the center is Oliver Schroeder Jr., professor of law at Western Reserve. He shares the administrative responsibilities with Dr. Samuel R. Gerber, coroner of the county since 1936; Dr. Alan Moritz, professor of pathology in the medical school and director of the institute of pathology; and George W. O'Connor, scientific investigator in the coroner's office and clinical instructor in criminology at the university.

"To utilize medicine and allied sciences as a source for the administration of civil and criminal justice requires organized planned research," Mr. Schroeder says. "Medicine is a pioneer in such activity; law is a new convert. . . . Medicine as represented by the mental and physical aspects of

Representatives of medicine, the law, and government share administrative responsibility for the Law-Medicine Center sponsored jointly by Western Reserve University and Cuyahoga County, Ohio.

the human body has a long historical relationship with the law. Ancient Jewish law recognized mental and physical elements of truth for law-giving. . . . The greatest growth of medicine as a source of truth for law has been within the last century, even the last decade. A law-medicine center is express recognition of such growth."

The Law-Medicine Center was opened shortly after voters authorized construction of the coroner's laboratory. Prior to this, Dr. Gerber and other persons had labored for several years to win public support for the idea that a coroner's office best fulfills all its purposes in a university setting. The current annual budget of the center is $40,000 and comes primarily from tuition fees.

In its seven years, the center has sponsored 52 schools or separate courses of instruction, in which enrollment has totaled 2,500 persons. Thirty-six of the schools have been in the field of criminal justice, enrolling over 1,300 policemen, prosecutors, coroners, medical examiners, and others interested in law enforcement. About one-fourth of the enrollment has been in the suburban police school, for officers from 56 municipalities in Cuyahoga County outside Cleveland. Most of them have departments too small to conduct extensive training for their own men, but together they serve an area of nearly 400 square miles and a population of 600,000. Separate schools are held for recruits and experienced policemen. The subject matter is the same, but the emphasis differs.

Medicine for Police

Physicians give part of the instruction at the schools, which run for one month, full time. How should a police officer administer first aid? How should he handle the mentally ill? How should he act in an obstetric emergency? How does he distinguish between alcoholic intoxication and diabetic coma? These are part of the subject matter covered by doctors.

They also have a teaching role in seminars on science in law enforcement, a more advanced course lasting one week. Psychiatrists lecture on child development and on delinquency-provoking influences in the adolescent. A pathologist describes the physiology of intoxication. An attorney presents some of the problems arising when 20th-century chemical tests clash with 18th-century personal rights.

In the area of civil justice, the center has sponsored 16 seminars or courses, enrolling nearly 1,200 lawyers, doctors, workmen's compensation specialists, insurance examiners, and others. Most recently completed was a course on "The Mentally Disabled and the Law," held for two hours every Monday night for 15 weeks. A two-day institute on "The Back: A Law Medicine Problem Reappraised" will be held Feb. 12-13. As part of the program, two damage settlement negotiations will be heard, one over a whiplash injury and the other over a disk injury. Previous seminars have been held on other specific parts of the body, including the heart, the head, and the extremities, as well as on more general medical issues in civil litigation.

Tools Versus Training

A man never becomes a doctor by being provided with stethoscope, white coat, and prescription pad—but often he becomes a policeman by being handed a badge and a gun.

Oliver Schroeder Jr., director of the Law-Medicine Center at Western Reserve University, cites these two examples as a plea for improved training standards in law enforcement.

"The garb and tools of the profession," Mr. Schroeder says, "must be reserved for those who exhibit a deep interest, understanding, and ability for the disciplines of that profession." He suggests that states may set stronger standards for police selection in smaller communities.

Police at the Law-Medicine Center receive part of their specialized training from physicians.

Other functions of the center have been publishing and research. Much of the material covered in the schools and seminars has been printed in books, monographs, and articles. A study was made of the 662 homicides investigated by the Cuyahoga County coroner over a seven-year period, bringing out legal, medical, and social factors.

Despite gains in cooperation between medicine and law toward the common goal of improved administration of justice, Mr. Schroeder predicts that friction between the professions will increase because of the growing complexity of society.

"The first problem," he says, "is to understand better the differences between the two professions." What are some of these differences which lead to misunderstanding? One is the adversary system used in courts of law. Both sides in a controversy present their viewpoints in the strongest manner. To the lawyer, such procedures are the best means of resolving conflicts between two persons when negotiated settlement is impossible. Doctors, on the other hand, find that such procedures are foreign and distasteful rather than a way to the truth.

Likewise, the two professions often have a different view of "cause" as it applies to the ill health of a patient or client. The lawyer finds cause to be crucial, since a plaintiff cannot legally recover damages unless it is determined. The doctor, however, may, in diagnosing a patient's ill health, be unable to determine one single "cause," even though he may be able to cure or alleviate the illness.

The basic purpose of a law-medicine center, Mr. Schroeder says, must go beyond settlement of present conflicts in which doctors may be accused of a "conspiracy of silence" or lawyers of "selling justice." Practical goals of the center will change as contemporary needs change, he says, but "The philisophical purpose is ageless—to acquire truth for the administration of justice."

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

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NEW DRIVE FOR COMPULSORY HEALTH INSURANCE

ONCE again in United States history compulsory federal health insurance is being debated by both political parties. No physician in the nation can afford to be complacent or unknowing in the midst of these portentous developments.

Agitation for enactment of a federal, compulsory health insurance program began in this country during the years 1934 to 1936, when the Social Security Act was proposed and enacted. Compulsory health insurance then, as now, was proposed as an integral part of Old Age and Survivors Insurance under Title II of the Social Security Act. Franklin Roosevelt, however, did not support the bill because he felt that it was too radical.

Years passed without any important political pressure for compulsory health insurance until the election of Mr. Truman in 1948. Soon thereafter the Truman administration supported the Wagner-Murray-Dingell bills, an earlier and more comprehensive version of today's Forand bill. The fight was on, and a bitter controversy it became. In the political campaigns of 1950, some of the principal proponents went down to defeat: Thomas in Utah, Pepper in Florida, Graham in North Carolina, Biemiller in Wisconsin, and others. Finally, the Truman administration, in an effort to eliminate the controversial issue from the campaigns of 1952, appointed a special commission to study the health needs of the nation.

Now, after 10 years, the same issue in the form of the Forand bill, introduced by Amie Forand (Democrat) and strongly supported by the AFL-CIO, has raised its head again. No matter what the year—1937, 1950, 1960—the issue remains the same.

The proponents of compulsory health insurance contend basically that the people—in this case social security recipients—should not be permitted to buy their own health care. The federal government, they contend, should purchase such benefits for them through taxes collected via the social security mechanism. The opponents of such legislation, on the contrary, support the basic principle that people should be permitted to choose freely how they wish to spend their own money. They urge programs to promote prosperity, maintain the purchasing power of the dollar, support the indigent, develop voluntary health insurance, and construct special facilities designed to meet the health needs of the aged, encourage home care, and other appropriate measures.

Actually, how serious a problem do those aged over 65 years face in meeting their health care needs? What is their economic status?

The full answer to these questions is not available, but from the Federal Social Security Administration has come a series of statistical analyses that have been adroitly exploited by Forand bill supporters.

A typical example of a misleading statistic widely quoted is the statement[1] that "Three-fifths of all people 65 and over had less than $1,000 in money income in 1956 and 1957." The fact is that "income per person" taken out of context does not present a true picture of the economic status of the individual person, especially the retired aged person. It does not take into account family and nonmonetary income, total assets, other resources, and the reduced financial obligations of the aged person.

In a recent article[2] in THE JOURNAL the authors pointed out that the Federal Reserve Board's annual sample Survey of Consumer Finances reveals that the liquid assets of persons aged 65 years and over have grown faster than the assets of any other age group in the last 10 years.

Generally speaking, the proportion of those over 65 years of age who have $2,000 or more or $5,000 or more is higher than for any other age group. And it should be noted that these "liquid assets" exclude homes, other real estate, and stocks and bonds other than savings bonds. The inclusion of these additional assets would make the discrepancy between those aged over 65 years and younger age groups even greater.

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[1] Report of the Secretary of Health, Education, and Welfare to the Committee on Ways and Means, April 3, 1959, United States Department of Health, Education, and Welfare, p. 8.

[2] Kemp, A.; Martin, L. W.; and Harkness, C.: Some Observations on Financial Assets of the Aged and Forand-Type Legislation, **171**: 1228-1231 (Oct. 31) 1959.

[3] Shanas, E.: Financial Resources of the Aging, Health Information Foundation, Research Series 10, November, 1959.

Another recent study,[3] from the Health Information Foundation, showed that the group over 65 years of age is as heterogeneous as other age groups in our nation. Many are rich, many are poor, and the majority are in between. When asked the question, "How would you meet a bill of $500 for medical care?", 82% answered that they would meet it in whole or in part from savings, current income, life insurance, mortgages, health insurance, or children and relatives. Only 18% indicated that they would have to rely on public assistance or charitable aid.

It is obvious that whatever problem exists is among the needy and near-needy aged who would be rapidly reduced to a state of destitution by prolonged illness. In recognition of this fact the Boards of Trustees of the American Medical Association and the American Hospital Association recently adopted a resolution dedicating their full resources to accelerate the development of adequately-financed health care programs for needy persons, especially the aged needy. Both organizations stated that "the indigent or near indigent is primarily a community responsibility." The resolution pointed out that the Forand bill fails to meet the need of the indigent aged since the vast majority of such aged are not eligible to receive social security benefits.

The Forand bill is a costly, irreversible program tailored to avoid the real problem. It is a fundamental deviation from the basic concept of the social security system which provides cash benefits, not services. It injects the federal government into the physician-patient-hospital relationship. Its enactment would be followed by control of the health care of the aged by the Social Security Administration.

The strongest objection, however, to this kind of legislation is that it is unnecessary and would lower the quality of care rendered. Great progress is being made through voluntary enterprise supplemented by governmental programs that do not socialize the health professions. Voluntary prepayment plans and health insurance have made phenomenal advances during recent years. Already 43% of those aged over 65 years are covered by some kind of insurance, and it is predicted that by the end of 1960, about 60% of those over 65 who wish to purchase such insurance will be covered. Social security cash benefits, private pension plans, increasing savings, and liquid assets are all combining to improve steadily the economic resources and purchasing power of the group over 65. Medical-care programs for indigent citizens, especially those over 65, are improving. A new psychological climate for the aging is being created that promotes their productive utilization in society. New hospital designs more suitable and more economical for the care of the ambulatory aged, homemaker services, home-care services, improved nursing homes, and other positive action programs are proceeding at a rapid pace. Thus, voluntary and governmental enterprise that preserve individual responsibility and free choice have teamed up in recent years and are moving rapidly to resolve whatever problems still remain.

It will always be possible to do a better job, but the one development which would apply a brake to all of these progressively developing movements would be Forand-type legislation. To bureaucratize medical care by funneling its services through the social security system would supply a "cure" that would be worse than the disease in its ultimate effects on individual freedom and a free society.

THE ELEMENTS OF STYLE

Few physicians who contribute regularly to medical journals or who profess an inborn flare for composition, even though their contributions rarely reach the printer's ink and paper stage, are perfectionists in composition. A perfectionist by my definition is one so gifted in the art of writing and so wise on the subject selected that the first copy is clean, tells the story as the writer desires the story to be told, and, except for the checking of references and the preparation of figures or tables is ready for editorial decision. There are a few contributors to American medical periodicals who have demonstrated their ability to make the first draft the final draft. Paul D. White, cardiologist to the President, a cyclist for his own pleasure, and a friend of the multitudes, is a writer capable of performing in near-perfect fashion. There are a favored few so endowed with talent of composition and selection of words that the copy is faultless by the second or third revision. The majority of us, however, must struggle through revision after revision, draft after draft, to achieve the goal. The final product should be pleasing to the ear as well as to the eye. The statements should be factual and the manuscript only long enough to cover the subject without repetition.

Most physicians attended medical school to acquire a medical education and not to prepare medical manuscripts. If the reverse were true, there would be a renaissance in medical literature while the practice of medicine would be in a grievous

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1. Strunk, W., Jr.: Elements of Style, New York, the Macmillan Company, 1959.

state. Fortunately a happy compromise is possible. Quality of medical writing can be improved without reducing quality of medical practice.

We rely on aids to help us in the pursuit of our profession. Too often, we fail to use aids in the preparation of medical manuscripts—aids that are readily available. One of the most useful is a book or books on style and composition. Some are ponderous and helpful only to the teacher of English composition. Others make delightful reading for anyone with an interest in improving this attribute. A small volume published recently and now a best seller throughout the United States is entitled "The Elements of Style."[1] This vest-pocket manual tells its story in 71 pages. Such old chestnuts as the split infinitive and the use of very, most, literally, and get are discussed. There is a chapter on elementary principles of composition and a concluding chapter on an approach to style. If the medical writer were to devote a few minutes of precious time to the perusal, assimilation, and digestion of the contents of this little book during the preparation of a manuscript, medical literature would be the gainer and the writer would be as delighted with his results of composition as with his revelation of scientific data.

J. H. T.

THE FIFTY-SIXTH CONGRESS ON MEDICAL EDUCATION AND LICENSURE

The program for the forthcoming Congress on Medical Education and Licensure is published in this issue of The Journal, pages 347 and 348. That portion of the Congress sponsored by the Council on Medical Education and Hospitals will focus attention on three issues of great significance to medical education. The transmission and storage of knowledge and the continuing search for truth through research are traditional and appropriate functions of all institutions of higher education. The provision for medical care is not in as high a priority category of university tradition. Nonetheless, the requirements of teaching and research in the clinical disciplines inevitably involve universities and their medical schools in the process of patient care.

Medical school faculties properly exhibit concern lest the demands of patient service weaken the primary objectives of education and research. However, patients enter teaching hospitals because they are ill and seek relief from discomfort and cure of disease. It is not a usual experience to encounter a patient desiring admission to a hospital for the primary purpose of contributing to an educational program. From the patient's viewpoint, it is of paramount importance that the teaching and research functions do not take precedent over skilled diagnosis and treatment. The Council's program will probe into circumstances under which the two activities—education and patient care—are likely to become disparate and also into circumstances that foster a complimentary relationship between them.

The late Abraham Flexner counseled wisely that medicine would grow strong only with its education rooted firmly in a university environment. The university orientation of medical education in this country is now such an accustomed belief that little thought is given to its true meaning. What are the characteristics of an educational institution that is worthy to be entitled a university? What values does a medical school gain from and contribute to a university? The concept of medicine as a university study will form an important part of the forthcoming Congress. This year marks the 50th anniversary of the publication of Abraham Flexner's report, and since his work contributed so vitally to the transfer of medical study to the university, this portion of the program will be dedicated to Flexner.

Over the years the inherent attractions of a medical career has allowed medicine the luxury of choosing the fortunate few from among the many young people who desired to become physicians. The rapidly changing scene of recent times has emphasized vividly the exciting challenges as well as the intellectual and worldly satisfactions to be found in many other careers. The identification and development of talented minds is one of today's vital issues. The Congress will present the problem of recruitment for medicine against the background of the general competition for intellectual talent.

These are matters of importance to all of medicine. The Congress on Medical Education and Licensure will provide an opportunity to consider them with participants who will present thoughts rich in experience and knowledge.

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FIFTY-SIXTH ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS, AMERICAN MEDICAL ASSOCIATION
and
ADVISORY BOARD FOR MEDICAL SPECIALTIES
and
FEDERATION OF STATE MEDICAL BOARDS OF THE UNITED STATES

Palmer House, Chicago
February 6-9, 1960

Registration

Saturday, Feb. 6, 10:30 a.m. to 5:00 p.m.
Sunday, Feb. 7, 8:00 a.m. to 5:00 p.m.
Monday, Feb. 8, 8:00 a.m. to 5:00 p.m.
Tuesday, Feb. 9, 8:00 a.m. to 12 noon

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Sunday, Feb. 7, Grand Ball Room

The Role of Patient Care in Basic Medical Education

Leland S. McKittrick, M.D., *Presiding*

9:15- 9:30 Chairman's Address
Leland S. McKittrick, M.D., Chairman, Council on Medical Education and Hospitals, American Medical Association

9:30-10:00 Medical Service as a Medical School Function
Arthur Richardson, M.D., Dean, Emory University School of Medicine

10:00-10:30 Care of the Patient in the Medical School Setting
Edmund Pellegrino, M.D., Chairman, Department of Medicine, University of Kentucky School of Medicine

10:30-11:00 The Patient, The Physician-Teacher, and the Student
R. C. Dickson, M.D., Chairman, Department of Medicine, Dalhousie University Faculty of Medicine

11:00-11:10 Intermission

11:10-11:30 Learning the Physician-Patient Relationship: Viewed in Retrospect by the 1950 Class
Helen Hofer Gee, Ph.D., Director of Research, Association of American Medical Colleges

11:30-12:00 A Patient Looks at the Medical School Hospital
Guy Hayes, M.D., Assistant Director, Division of Medical and Natural Science, The Rockefeller Foundation

12:00-12:30 Interprofessional Relationships in the Hospital: Their Impact on the Patient and the Medical Student
Leo W. Simmons, Ph.D., Executive Officer, Institute of Research and Service in Nursing Education, Teachers College, Columbia University

Advisory Board for Medical Specialties
The Role of Patient Care in Education Beyond Medical School

Ernest L. Stebbins, M.D., *Presiding President*, Advisory Board for Medical Specialties

2:00- 2:30 Clinical Education as a Continuum
Samuel Martin, M.D., Chairman, Department of Medicine, University of Florida College of Medicine

2:30- 3:00 Developing the Young Physician's Responsibility and Judgment in Patient Care
William Holden, M.D., Chairman, Department of Surgery, Western Reserve University School of Medicine

3:00- 3:30 The Effect of House Staff Training Programs on Patient Care
James Bordley III, M.D., Mary Imogene Bassett Hospital, Cooperstown, N. Y.

3:30- 3:45 Intermission

3:45- 4:15 The Ambulant Patient's Contribution to the Education of Interns and Residents
William D. Loeser, M.D., Youngstown (Ohio) Hospital Association

4:15- 4:45 Continuation Education in Hospitals Without House Officers
George Robertson, M.D., Thayer Hospital, Waterville, Maine.

Monday, Feb. 8, Grand Ball Room

Medicine as a University Study

Dedicated to Abraham Flexner, Sc.D.

> *Before the gates of excellence the high gods have sweat. Long is the road thereto, and rough and steep at the first. But when the height is achieved, then there is ease, though grievously hard in the winning.*—Hesiod

From the title page of "I REMEMBER"—the autobiography of Abraham Flexner

W. Clarke Wescoe, M.D., *Presiding Vice-Chairman*, Council on Medical Education and Hospitals

9:15- 9:45 The Lasting Ideals of Abraham Flexner
Lewis L. Strauss, President, Institute for Advanced Study, Princeton, N. J.; Former Chairman, Atomic Energy Commission; former Secretary of Commerce

9:45-10:15 The Hallmarks of University Education
Nils Wessell, Ph.D., President, Tufts University

10:15-10:45 The Medical Sciences: a Source of Scholarly Strength for the University
Stanley Bennett, M.D., Chairman, Department of Anatomy, University of Washington School of Medicine

10:45-11:00 Intermission

11:00-11:30 **The University: a Source of Scholarly Strength for the Medical School**
John S. Millis, Ph.D., President, Western Reserve University

11:30-12:00 **Medicine as a True University Graduate Study: Fact, Fiction, and the Future**
Maurice Visscher, M.D., Chairman, Department of Physiology, University of Minnesota Medical School

12:00-12:30 **Medicine's Debt to Abraham Flexner**
Louis Orr, M.D., President, American Medical Association

Looking Toward Tomorrow's Medical Student

Leland S. McKittrick, M.D., *Presiding*

2:00- 2:30 **Competition for the Talented Mind**
M. H. Trytten, Ph.D., Director, Office of Scientific Personnel, National Academy of Sciences–National Research Council

2:30- 3:00 **The Quantitative Problem: Providing Physicians for a Growing America**
Frank Bane, Chairman, USPHS Surgeon General's Consultant Group on Medical Education

3:00- 3:30 **New Faces for a New Era in Medicine**
Raymond Bunge, M.D., Chairman, Admissions Committee and Professor of Urology, State University of Iowa College of Medicine

3:30- 3:45 **Intermission**

3:45- 4:15 **Medicine's Attractions and Distractions**
C. Henry Kempe, M.D., Chairman, Department of Pediatrics, University of Colorado School of Medicine

4:15- 4:45 **Responsibility for Recruitment**
James Z. Appel, M.D., Director, Health Department, Franklin and Marshall College, Lancaster, Pa.; Member, Board of Trustees, American Medical Association

4:45- 5:15 **Career Information Materials**
Film: I Am a Doctor
Walter S. Wiggins, M.D., Secretary, Council on Medical Education and Hospitals, American Medical Association

Saturday, 2:00 p.m., Room 14

Federation of State Medical Boards of the United States

2:00- 5:00 **Annual Examination Institute**
Biochemistry—Medicine and Diagnosis
Exercises in Question Construction

Sunday, 2:00 p.m., Room 14

Federation of State Medical Boards of the United States

2:00- 3:00 **Annual Meeting**
- Roll Call
- Report of Secretary-Treasurer
- Appointment of committees
- Reports of Officers
- Resolutions
- Nominations
- Others
- Reports of Committees
  - Examination Institutes, 1959
    Stiles D. Ezell, M.D., Chairman
  - Public Relations
    M. H. Crabb, M.D., Chairman
  - Educational Council for Foreign Medical Graduates
    Elmer W. Schnoor, M.D., Trustee
  - Legislative
    S. M. Poindexter, M.D., Chairman
  - Constitution and Bylaws
    Clyde M. Swett, M.D.
  - Study of Paramedical Areas in Relation to Medicine
    Lall G. Montgomery, M.D.
  - Internship Review
    C. J. Glaspel, M.D.

3:00- 3:30 **The Physician and Medical Literature**
S. S. B. Gilder, M.D., Editor, Canadian Medical Journal

3:30- 5:00 **Panel: Current Attitudes on Discipline in:**
Abortions—Lewis P. Gundry, M.D., Maryland
Narcotic Addiction, John F. Fiorino, M.D., Washington
Mental Illness in the Physician, R. C. Derbyshire, M.D., New Mexico
Income Tax Evasion and Other Felonies, Albert M. Deal, M.D., Georgia
Unprofessional Conduct: Lall G. Montgomery, M.D., Indiana

8:00-10:00 **Annual Conference of Secretaries of State Medical Boards**
M. H. Crabb, M.D., Chairman, Public Relations Committee

Monday, 6:30 p.m., Crystal Room

Federation of State Medical Boards of the United States

6:30- 8:00 **Annual Federation Dinner**

8:00- 9:00 **Fifth Annual Walter L. Bierring Lecture**
Louis Orr, M.D., President, American Medical Association

Tuesday, 9:00 a.m., Red Lacquer Room

Federation of State Medical Boards of the United States
International Medical Education

Edwin H. Lawson, M.D., *Presiding*

9:00- 9:30 **Medical Education: A Study in Comparative Values**
Edwin H. Lawson, M.D., *President*, Federation of State Medical Boards of the United States

9:30-10:00 **Obstacles in Medical Education at the International Level**
John M. Weir, M.D., Associate Director, Division of Medical and Natural Sciences, The Rockefeller Foundation

10:00-12:00 **Panel: Aspects of International Medical Education:**
The Selection of Students
Ernavi Braga, M.D., Brazil
What is Attempted in the Basic Medical Sciences
Yoh Nakagawa, M.D., Japan
The Approach to Clinical Orientation
Jose Cara, M.D., Brazil
Clinical Clerkships
Eduardo Ferraco, M.D., Brazil
The Internship
Ambhan Dasaneyavaja, M.D., Thailand
Postgraduate Qualification
Wolfgang Goetze-Claren, M.D., Germany

Tuesday, 12:30 p.m., Crystal Room

Federation of State Medical Boards of the United States

12:30- 1:30 **Annual Federation Luncheon**
1:30- 3:30 **Annual Business Meeting**

MEDICAL NEWS

ALASKA

State Convention in Anchorage.—The Alaska State Medical Association will meet Feb. 18-20 in Anchorage. Dr. Louis M. Orr, President, American Medical Association, will present "Cancer of the Prostate" at an afternoon session and will also be main speaker at the banquet. Dr. Fount Richardson, Fayettesville, Ark., president, American Academy of General Practice will also be a banquet speaker and will give a scientific presentation. Other speakers on the program are listed as follows: Dr. Rodman Wilson, Anchorage; Dr. James W. Miller, Seattle; Dr. John R. Schenken, Omaha; Dr. Julius L. Wilson, New York City; Dr. Herbert E. Griswold Jr., Portland, Ore.; Dr. John W. Cashman, Kansas City, Mo.; Paul A. Younge, Boston; and Dr. George A. Adams, Atlanta, Ga. A team from the National Institutes of Health will give several talks with illustrations. For information, write Dr. Michael F. Beirne, 835 I St., Anchorage, Alaska, Chairman, Committee on Publicity.

ARKANSAS

Annual Institute in Psychiatry and Neurology.—The 12th annual Institute in Psychiatry and Neurology will be held Feb. 25-26 at the North Little Rock Division of the Consolidated Veterans Administration Hospital. In addition to two days of scientific presentations, there will be four related conferences on Feb. 24 in clinical psychology, psychiatric social work, psychiatric nursing, and dietetics. Social events include a dinner on Thursday evening, Feb. 25, with Dr. Mathew Ross, Washington, D. C., as guest speaker; a ladies' luncheon on Friday; and also on Friday the Fort Roots Medical Association luncheon. There is no charge for registration. For information, write Dr. Harold W. Sterling, Manager, Veterans Administration Consolidated Hospital, Little Rock, Ark.

CALIFORNIA

Regional Meeting of Physicians.—The Southern California Regional Meeting of the American College of Physicians will be held Feb. 6-7 at the Hotel Del Coronado in Coronado. The program includes over 30 papers to be presented in addition to 12 to be read by title. Dr. Howard P. Lewis, Portland, Ore., president of the college, and president-elect, Dr. Chester S. Keefer, Boston, will be guests of honor, and Dr. Keefer will present "The Problem of Chronic Bronchitis" the afternoon of Feb. 6. A dinner dance is planned for 7:30 p. m., Feb. 6. For information, write the American College of Physicians, 4200 Pine St., Philadelphia 4.

Annual Session in Los Angeles.—The 89th annual session of the California Medical Association will be held in Los Angeles, Feb. 21-24, with headquarters at the Ambassador Hotel. The association cancer commission will hold preconvention conferences on radiology and pathology Feb. 20. Guest speakers at the annual session will include Drs. Lauren V. Ackerman, St. Louis; Oliver Cope, Boston; Albert Segaloff, New Orleans; and William B. Wood Jr., Baltimore. Special guests of sections will include Dr. Johnnie R. Betson Jr., Albuquerque, N. M., and Dr. Warren Palmer Dearing, Washington, D. C. General meetings will be held Feb. 22 and 23, with a special meeting planned for the morning of Feb. 23. Symposiums will be held on the following topics: Parathyroid Disorders—Diagnosis and Treatment, The Management of Advance Malignant Disease, and Disaster Medical Care. A clinical pathological conference is planned for the afternoon of Feb. 23. Postgraduate courses, technical and scientific exhibits, and a program of medical motion pictures are planned. A ladies' program is arranged. For information, write Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

COLORADO

Rocky Mountain Surgical Meeting.—On Jan. 28-30 the Rocky Mountain Surgical Society will meet in Aspen. Of the 15 papers scheduled for presentation, the following will be given by out-of-state speakers:

Salvaging Pollicization, Dr. James Gmeimer, Appleton, Wis.
Management of Severe Hand Injuries, Dr. David W. Robinson, Kansas City.
The Management of Medical and Surgical Emergencies in Primitive Areas, Dr. DeWitt Dominick, Cody, Wyo.
Ruptured Eardrum, Dr. John J. Shea Jr., Memphis, Tenn.
Water Skiing Hazards, Dr. Ernest M. Burgess, Seattle.
Dynamic Posture, Dr. M. Beckett Howorth, Stanford, Conn.

Movies will be shown two days. A banquet will be held Jan. 30, 7:30 p. m. For information, write Dr. Charles S. Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

CONNECTICUT

Dr. Long Honored.—Dr. Cyril N. Hugh Long, Sterling Professor of Physiology and chairman of the department of physiology at Yale University

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

School of Medicine, New Haven, was honored Dec. 8 when he received the 1959 Pharmaceutical Manufacturers Association Award for "outstanding contributions in the field of medicine." Among Dr. Long's research is his work on the importance of various endocrine glands, particularly the adrenal, in diabetes; his investigations on carbohydrate metabolism; and his studies on the physiological theory of muscle activity.

GEORGIA

Meeting on Clinical Hypnosis.—On Jan. 10 the first quarterly meeting of the Georgia State Society of Clinical Hypnosis was held at the Academy of Medicine, Altanta. The state society is a unit of the American Society of Clinical Hypnosis. The following Atlanta physicians were speakers on the program: Dr. Trajan E. Shipley, Dr. Harry R. Lipton, and Laurence Bryan, Ph.D. For information, write Dr. Clifton G. Kemper, 117 Doctors Building, 478 Peachtree St., N. E., Atlanta, Ga.

ILLINOIS

Award for Paper by Psychiatric Resident.—The Illinois Psychiatric Society announced that it will present an award of $100 to the psychiatric resident presenting the "best original paper" on a psychiatric research problem. Author of the paper must be a resident physician in training at an approved psychiatric facility in Illinois. Papers must be submitted to the society by April 1. The award paper will be presented to the society at a fall meeting. A special committee has been appointed to make the selection of the award: Dr. Lester H. Rudy, Galesburg, chairman, Dr. Joseph G. Kepecs, Dr. C. Knight Aldrich, Dr. Joel S. Handler, ex-officio, Dr. Frances Hannett, ex-officio, Chicago. The address of the society is 1601 W. Taylor St., Chicago.

Chicago

Concert to Benefit Research.—On behalf of the Mount Sinai Medical Research Foundation, Van Cliburn will play on Monday evening, March 7, at the Civic Opera House. The Mount Sinai Hospital Service Club, an organization of 415 Chicago ladies, has taken over the entire house as a benefit in behalf of the foundation at Mount Sinai Hospital. Benefit proceeds will help to finance research being conducted at the Mount Sinai Medical Center on cancer, leukemia, the Rh factor, and diseases of the blood. For information, write the Mount Sinai Hospital Service Club, 920 N. Michigan Ave. (CRawford 7-4551).

Appoint Chairman of Microbiology Department.—The appointment of James W. Moulder, Ph.D., as chairman of the department of microbiology of the University of Chicago effective July 1 was announced by Dr. Lowell T. Coggeshall, dean of the university's Division of Biological Sciences. Dr. Moulder will succeed William D. Taliaferro, Ph.D., who retires as the Eliakim Hastings Moore Distinguished Service Professor as well as chairman of the department of microbiology. Professor of microbiology since 1957, Dr. Moulder has been a member of the faculty of the University of Chicago since 1944. He is joint editor of the *Journal of Infectious Diseases.* He held Guggenheim and Fulbright fellowships to Oxford University, England, in 1952-1953 and received the Eli Lilly Award in Bacteriology, Immunology and Pathology in 1954.

New Tuberculosis Clinic.—The board of directors of the Municipal Tuberculosis Sanitarium announced that on Dec. 18 the clinic services would be discontinued at the present location in the Provident Hospital and will be moved to 3525 S. Michigan Ave., at which location construction of a new clinic building has been completed. The new building will be known as the Ernest E. Irons Clinic in memory of the late president of the board of directors. This new tuberculosis clinic opened Dec. 23 replacing the old MTS-Provident and MTS-Mercy Clinics. Physicians and agencies are invited to refer patients for tuberculosis services. Chest x-rays are taken on persons over 15 years of age and on positive reactors under 15. All services are free. This clinic serves the area bounded on the north by 18th Street; on the south by 67th Street; on the east by the lake; and on the west by Wentworth Avenue (200 W.). Patients should be referred Monday through Friday inclusive from 9 a. m. to 11:30 a. m. and from 1:00 p. m. to 4:30 p. m.

MARYLAND

Leprosy Research Laboratory at Johns Hopkins.—The establishment of a laboratory for leprosy research at the Johns Hopkins University School of Hygiene and Public Health, Baltimore, was announced Jan. 9 by Milton S. Eisenhower, D.Sc., president of the university, and Cyril I. Crowther, president of the Leonard Wood Memorial (American Leprosy Foundation). The laboratory, which succeeds one that had been maintained by the memorial for the past 13 years at the Harvard Medical School, Boston, will be financed by the memorial, aided by a grant from the National Institute of Allergy and Infectious Diseases of the U. S. Public Health Service. John H. Hanks, Ph.D., bacteriologist of the memorial for the past 20 years and now associate professor of pathobiology at the School of Hygiene, will be director of the laboratory. A formal opening ceremony for the laboratory was held on Jan. 13, with addresses by Dr. Willard C. Rappleye, president of the Josiah Macy Jr., Foundation of New York, and Dr. James A. Doull, medical director of the Leonard Wood Memorial. The Leonard Wood Memorial established in 1928, was named after Maj. Gen. Leonard Wood, American soldier, physician, and statesman who became interested in leprosy while serving as governor of the Philippines.

MASSACHUSETTS

Course for School Physicians.—Dr. Sidney S. Listernick, Everett, president, Massachusetts School Physicians' Association, announced that arrangements have been made for a short course for school physicians to be given in the Jimmy Auditorium, Children's Medical Center, Boston, Wednesday afternoons, 2 to 4 p. m., on April 27 and May 4, 11, and 18. The following content of the course has been approved:

1. Handicaps requiring special educational adjustment.
2. The clinical outcome of the school child's periods of stress and mental health facilities and service available to assist in the handling of these problems.
3. Environmental hazards to which the school child is subjected including accidents and employe health and injuries usually encountered in sports.
4. Adolescents from the point of view of the school physician.

For information, write Dr. Listernick at 37 Ferry St., Everett 49, Mass.

MINNESOTA

Dr. Bargen Retires.—Dr. Jacob Arnold Bargen, Rochester, a member of the staff of the Mayo Clinic for 33 years and head of a section of medicine and chairman of four sections of medicine, retired from active practice on Dec. 31. Dr. and Mrs. Bargen plan to go on an ocean cruise and Dr. Bargen will speak at the International Congress of Gastroenterology at Leyden, Holland, April 22, at the meeting of the International College of Surgeons in Rome, Italy, May 21, and other medical meetings in the United States in April. In 1941 and 1942 he was secretary of the American Gastroenterological Association and in 1950 he was chosen president of that group. In 1944 and 1945 he was chairman of the Section of Gastroenterology and Proctology of the American Medical Association, and he was a member of the council of the Minnesota State Medical Association from 1948 to 1958. Since 1957 he has been a member of the Council on Scientific Assembly of the A. M. A.

NEW MEXICO

Symposium on Problems of the Aged.—A statewide symposium on problems of the aged will be held in the Student Union Building at the University of New Mexico in Albuquerque Jan. 23-24. Principal speaker at the symposium, sponsored by the New Mexico Medical Society and the New Mexico Department of Public Health, will be Dr. Theodore G. Klumpp, New York City, member of the American Medical Association Committee on Aging. In addition to participating in the symposium, he will speak at a meeting open to the public at 8 p. m., Jan. 23. The program was planned by Dr. Samuel R. Ziegler, Espanola, past-president of the state medical society and chairman of the society's committee on aging; Dr. Stanley J. Leland, Santa Fe, director of the New Mexico State Health Department; and Dr. Molly Radford, Santa Fe, director of the state health department's division of gerontology.

Problems of the aged to be discussed include hospitalization, rehabilitation, financing for the aged, health care, community planning, group and community responsibility, housing, home makers services, nursing home services, and nursing care. The state medical society at its recent house of delegates meeting in Roswell approved a plan calling for a statewide conference on aging. It recommended that the state society and its county medical societies take the leadership on problems of aging, coordinating efforts with all interested groups in the field.

NEW YORK

Report on Upstate Poliomyelitis.—Dr. Herman E. Hilleboe, state health commissioner, said in a year-end summary of the poliomyelitis situation in Upstate New York that there were 264 cases of paralytic poliomyelitis, compared with 125 during 1958. The number of reported cases of poliomyelitis (both paralytic and nonparalytic) was 339, compared with 176 for 1958. The average number of cases reported for 1951-1953 was 1,666, with 959 cases paralytic. Dr. Hilleboe said that 130 of the paralytic cases had not received even one injection of antipoliomyelitis vaccine; 76 of the cases received three or more injections. Twenty-five deaths from poliomyelitis were reported during the year, with 18 occurring in persons who had less than three injections of the vaccine. Dr. Hilleboe said that there were 56 cases of paralytic poliomyelitis reported in the 20-39 age group. Of these, only four had three or more injections of the Salk vaccine. Ten of the twenty-five deaths occurred in the 20-39 age group.

Conference on Actinomycins.—A conference on "The Actinomycins and Their Importance in the Treatment of Tumors in Animals and Man" will be held under the auspices of the New York Academy of Sciences at the Barbizon-Plaza Hotel in New York City on Thursday, March 31, and Friday, April 1. Dr. Selman A. Waksman, of the Institute of Microbiology, Rutgers University, proposed the conference and will serve as conference chairman. The scientific program includes the following papers by foreign authors:

Structural Difference of the Actinomycins and Actinomycin Derivatives, Hans Brockmann, University of Gottingen, Gottingen, Germany.

Chemistry of Actinomycin D, Alan W. Johnson, University of Nottingham, Nottingham, England.

The Production of Actinomycin by Directed Biosynthesis, G. Schmidt–Kastner, Physiologischen Laboratorium, Farbenfabriken–Bayer, Germany.

Effect of Actinomycins upon Experimental Tumors, C. Hackmann, Institute for Experimental Pathology, Wuppertal–Elberfeld, Germany.

Clinical Experience with Actinomycin C, H. Begemann, Medizinischen University Klinik, Freiburg, i. Br., Germany.

Methods of Administration of Actinomycin in the Treatment of Different Tumors, A. Ravina and M. Pestel, Hospital Beaujon Clichy, France.

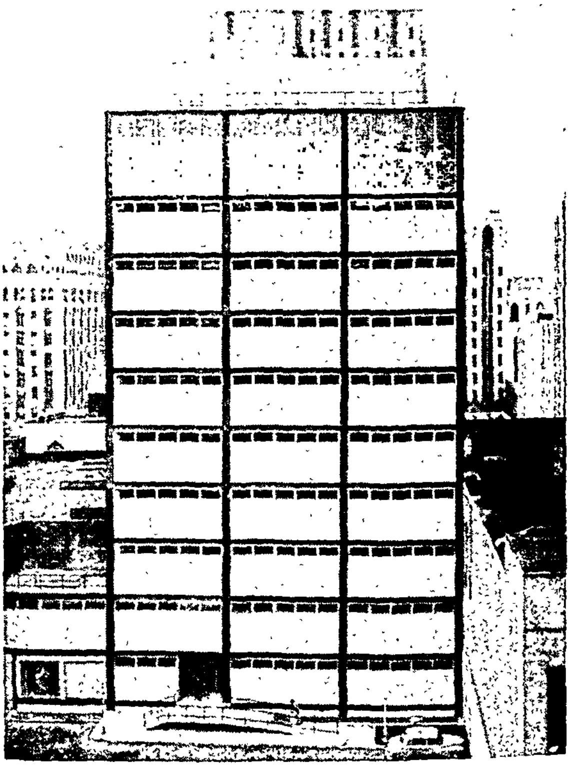
A dinner will be held the evening of March 31, after which an after-dinner address will be given by Dr. Waksman. Invitations to attend the conference will be issued to interested professional persons upon request. There is no registration for those attending. Requests should be addressed to the Executive Director, New York Academy of Sciences, 2 E. 63rd St., New York 21.

New York City

Name Two Tuberculosis Fellows.—Two fellowships were granted by the New York Tuberculosis and Health Association: Dr. Bella S. Strauss, a research fellow in the department of pathology at the New York University College of Medicine, has been awarded the James Alexander Miller Fellowship, established in 1949 as a memorial to the physician who was the first president and founder of the New York Tuberculosis and Health Association; Dr. Mallory Stephens, a fellow in medicine at the Albert Einstein College of Medicine, is the recipient of he New York Tuberculosis and Health Association Fellowship awarded this year for the first time. The Miller Fellowship carries a stipend of $7,000, whereas the association fellowship carries a grant of $5,000. Awarded as part of the association's $100,000 program to support research and scientific fellowships, they cover a one-year period beginning next July 1.

Tuberculosis in Children.—The New York Tuberculosis and Health Association, Inc., reported that while the number of tuberculosis cases and deaths in New York City continued their downward trend last year, the status of the diseases among children remained virtually unchanged. "Although they comprise a comparatively small number of cases, the number of children with active tuberculosis has remained relatively constant for several years, particularly among those under the age of five," according to the latest review of tuberculosis published by the association. There were 418 children under 5 with active disease on the tuberculosis register, maintained by the Health Department, as of Dec. 31 last year. On the same day, there were 259 children between the ages of 5 and 9 who had tuberculosis, and 117 between the ages of 10 and 14. The report also showed that 11 active cases of tuberculosis were found in the course of a routine tuberculin testing program conducted last year in the city's secondary schools. A total of 5,482 new cases of tuberculosis was reported in New York City for last year, and 833 deaths were attributed to this disease. The number of the new cases last year was 10% below that of 1957, while deaths in 1958 declined to an all-time low.

Institute for Research on Muscle Disease.—The Institute for Muscle Disease, Inc., a new medical research center, officially opened Dec. 12. The institute is reportedly the world's first research center devoted exclusively to the study of muscle and its pathologies. An 11-story structure housing laboratories, workrooms and special equipment, the institute fulfills a long-range objective of Muscular Dystrophy Associations of America, Inc. It was built at a cost of more than 5 million dollars through public contributions to the March for Muscular Dystrophy. Dr. Ade T. Milhorat, director of the new center, said its purpose is "to increase our knowledge of muscle, to understand the mechanisms by which muscular dystrophy and other muscular disorders arise, and to develop effective treatments for these conditions." When fully staffed, the institute will have some 150 research specialists and technicians working in such areas of study as physiology and biophysics, enzyme chemistry and microbiology, experimental pathology, protein chemistry, clinical investigation, and organic chem-



A rear view of the Institute for Muscle Disease, Inc.

istry. The institute's facilities include millicurie and microcurie "hot rooms" for work involving radioisotopes: two electron-microscope suites; germ-free quarters for experimental animals; a metabolism unit and living-in accommodations for patients cooperating in metabolic studies. The institute will also serve as a clearing house for information on muscle pathology. Ground-breaking ceremonies were held in October, 1957. The institute is located at 515 E. 71st St., New York City.

NORTH CAROLINA

Training Program in Psychiatry.—A new research training program in psychiatry is scheduled to be initiated at the Duke University Medical Center, Durham, this year. Purpose of the program is to provide more research scientists in the fields of mental health and disease. Financial support, scheduled to total $165,000 over a five-year period, has been allotted to Duke by the National Institutes of Health, principal research arm of the U. S. Public Health Service. Trainees in the program will be persons "with potentiality for research careers who hold the M.D. degree and who are engaged in or have completed their residency training in psychiatry." Dr. Ewald W. Busse, chairman of the Medical Center's psychiatry department, said that the two-year training period will include formal instruction, contacts with established investigators in psychiatry and other fields, participation in short-term and long-term research projects, and participation in conferences and seminars. The trainees will be designated fellows in psychiatric research. Two fellows will be admitted to the program during the first year, beginning July 1, three the second year, and four the third year. The program for each participant will be tailored to his interests and capabilities. A research training committee from the psychiatry faculty will select fellows, review their progress, and approve training plans submitted by the fellows and their advisors.

Personal.—On Dec. 5, at a meeting of the board of directors of the American Heart Association, Dr. Harold D. Green, professor of physiology and pharmacology, Bowman Gray School of Medicine, Winston-Salem, was presented a special award for "distinguished service to research." The special awards are a recently established policy of the American Heart Association and are presented to those individuals who have served on the Research Committee of the AHA for five full terms.——Dr. William L. Fleming, of the University of North Carolina School of Medicine, Chapel Hill, has been elected president of the Association of Teachers of Preventive Medicine. Dr. Fleming is chairman of the department of preventive medicine and assistant dean for education and research at UNC. The association was formed in 1954 and grew out of an informal organization started in 1942 known as the Conference of Professors of Preventive Medicine.——Norman M. Sulkin, Ph.D., director, department of anatomy, Bowman Gray School of Medicine, Winston-Salem, was elected and appointed to the following positions at the November meeting of the Gerontological Society at Detroit: chairman, section on biological sciences; senior member on the governing council, representing the biological sciences; and editorial board member, *Journal of Gerontology* and *Gerontological Newsletter*. He has been asked to serve as chairman of a Symposium on Neurology and Endocrinology at the fifth International Congress of Gerontology in San Francisco in August.

OHIO

Dr. Sabin to Visit Russia.—The Poliomyelitis Research Institute of the Soviet Academy of Medical Sciences, in Moscow, is planning a March 15-19 meeting in which Dr. Albert B. Sabin, poliomyelitis researcher for the University of Cincinnati and the Children's Hospital Research Foundation, will participate. Dr. Sabin will go to Russia early in March. This is in accord with the arrangements for United States-USSR scientific meetings in several medical fields begun during Premier Khrushchev's visit here in September. Chief consideration of the meeting will be Dr. Sabin's oral live poliomyelitis virus vaccine, which has undergone field tests involving millions of Russians this summer in the Soviet Union. Dr. Sabin will also address the Russian institute, presenting "The Eradication of Poliomyelitis as a World Problem." He has been notified that the USSR Ministry of Health has recommended his vaccine be given to about 60 million Russian children during the next few months.

OREGON

Surgical Meeting in Portland.—A sectional meeting of the American College of Surgeons will be held in Portland March 28-30 at the Sheraton Hotel. Dr. Millard S. Rosenblatt, Portland, associate clinical professor of surgery, University of Oregon Medical School, is chairman of the advisory committee on local arrangements. The program will include scientific reports, symposiums on injuries and cancer, and medical motion pictures and clinic films. A fellowship luncheon, at which activities of the college will be discussed, will be held at noon, March 29. Dr. Harry C. Blair, Portland, associate clinical professor, University of Oregon Medical School, will be the speaker at the college dinner, presenting "Anson G. Henry, Lincoln's Friend and Physician, Oregon Pioneer Doctor." Guest speakers from other states will include Drs. William P. Longmire Jr., Los Angeles; Leon Goldman, San Francisco; Thomas R. Sarjeant and Allan D. McKenzie, both from Vancouver; Frederic P. Shidler, Menlo Park, Calif.; Stanley O. Hoerr, Cleveland; and Walter S. Anderson, Edmonton. Panel discussions are planned. Dr. H. Prather Saunders, associate director, American College of Surgeons, 40 E. Erie St., Chicago 11, is in charge of all sectional meetings for the college.

PENNSYLVANIA

Physicians Meeting in Philadelphia.—The 21st annual reunion of Eastern Pennsylvania, a regional meeting of the American College of Physicians will be held at the Sheraton Hotel, Philadelphia, Jan. 30. Twenty-four papers are scheduled for presentation in addition to 20 papers which will be read by title. Dr. Howard P. Lewis, Portland, Ore., president of the college, will present "The Place of the American College of Physicians in American Medicine," at the banquet at 7 p. m. For information, write Dr. Edward C. Rosenow, 4200 Pine St., Philadelphia 4, Executive Director.

Hospital Named for Dr. Marcy.—The Pittsburgh State Tuberculosis Hospital was renamed the C. Howard Marcy State Hospital "in recognition of the service rendered by the late Pittsburgh physician in the fight against tuberculosis." The hospital has a population of 390 patients. Dr. George E. Martin has been its medical director for 24 years. Dr. Marcy's efforts in tuberculosis control covered a 43-year period. He was a member of the board of directors of the National Tuberculosis Association for 10 years and for eight years was president of the Pennsylvania Tuberculosis and Health Society. The C. Howard Marcy State Hospital is one of the four such institutions operated by the Pennsylvania State Health Department.

Philadelphia

Hospital and Medical School Affiliate.—The American Oncologic Hospital of Philadelphia entered into a scientific affiliation with 112-year-old Hahnemann Medical College and Hospital on Jan. 3. Dr. Paul J. Grotzinger Jr., associate professor of surgery at Hahnemann, was named medical director at Oncologic Hospital. Dr. Luther W. Brady Jr., associate professor of radiology at Hahnemann, was appointed chief radiation therapist. Oncologic Hospital medical staff members will be invited to join the Hahnemann faculty. Oncologic Hospital is a 56-bed hospital specializing in the care and treatment of patients with cancer and allied diseases. The institution's enlarged outpatient facility, the Dorrance Memorial Clinic constructed in 1954, offers diagnostic and treatment service for ambulatory cancer patients. The clinic is named in honor of the late Dr. George M. Dorrance, long associated with the institution as surgeon and medical director. Hahnemann Hospital will provide resident doctor coverage for Oncologic Hospital. There will be no change in the corporate identities or administrative structures of the two facilities.

UTAH

State Flying Physicians Organize.—At a recent meeting of the Utah Chapter of the Flying Physicians Association, Dr. L. Weston Oaks, of Provo, was elected chairman; Dr. Eugene N. Davie, of Milford, co-chairman; Dr. Donald K. Bailey, of Salt Lake City, secretary-treasurer; Dr. Charles H. Castle, of Salt Lake City, disaster chairman; and Dr. J. Eldon Dorman, of Price, chosen as weather and safety chairman. There are 21 M.D.'s in the State of Utah who are also active and certified pilots, most of whom are members of the Utah Chapter of the Flying Physicians Association.

GENERAL

Trauma Surgeons to Meet in California.—Dr. William T. Fitts Jr., Philadelphia, secretary of the American Association for the Surgery of Trauma, announced that the next annual meeting of the association will be Oct. 5-7 at the Hotel Del Coronado, Coronado, Calif., preceding the clinical congress of the American College of Surgeons, to be held Oct. 10-14 in San Francisco. Confusion has arisen as a result of erroneous dates being reported for the clinical congress of the college. For information on the trauma meeting, write Dr. Fitts, 3400 Spruce St., Philadelphia 4.

Surgeons Name Dr. North as Director.—Dr. John P. North, Dallas, Texas, will become the director of the American College of Surgeons, effective Jan. 31, 1961, Dr. Isidor S. Ravdin, Philadelphia, chairman, board of regents of the college, announced. Dr. North, who will succeed Dr. Paul R. Hawley, Chicago, the college's director since March, 1950, has been chief, Surgical Service, Veterans Hospital, Dallas, since 1955, and professor of clinical surgery at Southwestern Medical School of the University of Texas since 1946. He has been a fellow of the college since 1935 and a member of the board of governors since 1954.

New Fifty Year Club.—Dr. John H. McCurry, of Cash, Ark., is interested in forming an A. M. A. Fifty Year Club in which membership would be limited to members of the Association who have been in practice 50 years or more. The first meeting of the new club is expected to be held during the annual clinical meeting of the Association in Washington, D. C., in November, 1960. Those who are qualified and desire to join this organization are requested to so advise Dr. McCurry, giving their complete name and address. Dr. McCurry plans to be in Miami at the June meeting to begin organizational procedures and to see any who qualify at this meeting.

Society News.—The American Academy for Cerebral Palsy newly elected officers are as follows: Drs. Raymond R. Rembolt, Iowa City, president;

George W. N. Eggers, Galveston, Texas, president-elect; Herman Josephy, Chicago, vice-president, Joseph D. Russ, New Orleans, secretary, and Samuel B. Thompson, Little Rock, Ark., treasurer. The 1960 annual meeting will be held in Pittsburgh Oct. 5-8 at the Penn–Sheraton Hotel.— Officers for 1959-1960 of the **American Society of Ophthalmologic and Otolaryngologic Allergy** are: Drs Walter E. Owen, Peoria, Ill., president; Leland H. Prewitt, Ottumwa, Iowa, president-elect; Durward A. Skinner, Newark, Ohio, vice-president; and Daniel S. DeStio, Pittsburgh, secretary-treasurer

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PENNSYLVANIA

Physicians Meeting in Philadelphia.—The 21st annual reunion of Eastern Pennsylvania, a regional meeting of the American College of Physicians will be held at the Sheraton Hotel, Philadelphia, Jan. 30. Twenty-four papers are scheduled for presentation in addition to 20 papers which will be read by title. Dr. Howard P. Lewis, Portland, Ore., president of the college, will present "The Place of the American College of Physicians in American Medicine," at the banquet at 7 p. m. For information, write Dr. Edward C. Rosenow, 4200 Pine St., Philadelphia 4, Executive Director.

Hospital Named for Dr. Marcy.—The Pittsburgh State Tuberculosis Hospital was renamed the C. Howard Marcy State Hospital "in recognition of the service rendered by the late Pittsburgh physician in the fight against tuberculosis." The hospital has a population of 390 patients. Dr. George E. Martin has been its medical director for 24 years. Dr. Marcy's efforts in tuberculosis control covered a 43-year period. He was a member of the board of directors of the National Tuberculosis Association for 10 years and for eight years was president of the Pennsylvania Tuberculosis and Health Society. The C. Howard Marcy State Hospital is one of the four such institutions operated by the Pennsylvania State Health Department.

Philadelphia

Hospital and Medical School Affiliate.—The American Oncologic Hospital of Philadelphia entered into a scientific affiliation with 112-year-old Hahnemann Medical College and Hospital on Jan. 3. Dr. Paul J. Grotzinger Jr., associate professor of surgery at Hahnemann, was named medical director at Oncologic Hospital. Dr. Luther W. Brady Jr., associate professor of radiology at Hahnemann, was appointed chief radiation therapist. Oncologic Hospital medical staff members will be invited to join the Hahnemann faculty. Oncologic Hospital is a 56-bed hospital specializing in the care and treatment of patients with cancer and allied diseases. The institution's enlarged outpatient facility, the Dorrance Memorial Clinic constructed in 1954, offers diagnostic and treatment service for ambulatory cancer patients. The clinic is named in honor of the late Dr. George M. Dorrance, long associated with the institution as surgeon and medical director. Hahnemann Hospital will provide resident doctor coverage for Oncologic Hospital. There will be no change in the corporate identities or administrative structures of the two facilities.

UTAH

State Flying Physicians Organize.—At a recent meeting of the Utah Chapter of the Flying Physicians Association, Dr. L. Weston Oaks, of Provo, was elected chairman; Dr. Eugene N. Davie, of Milford, co-chairman; Dr. Donald K. Bailey, of Salt Lake City, secretary-treasurer; Dr. Charles H. Castle, of Salt Lake City, disaster chairman; and Dr. J. Eldon Dorman, of Price, chosen as weather and safety chairman. There are 21 M.D.'s in the State of Utah who are also active and certified pilots, most of whom are members of the Utah Chapter of the Flying Physicians Association.

GENERAL

Trauma Surgeons to Meet in California.—Dr. William T. Fitts Jr., Philadelphia, secretary of the American Association for the Surgery of Trauma, announced that the next annual meeting of the association will be Oct. 5-7 at the Hotel Del Coronado, Coronado, Calif., preceding the clinical congress of the American College of Surgeons, to be held Oct. 10-14 in San Francisco. Confusion has arisen as a result of erroneous dates being reported for the clinical congress of the college. For information on the trauma meeting, write Dr. Fitts, 3400 Spruce St., Philadelphia 4.

Surgeons Name Dr. North as Director.—Dr. John P. North, Dallas, Texas, will become the director of the American College of Surgeons, effective Jan. 31, 1961, Dr. Isidor S. Ravdin, Philadelphia, chairman, board of regents of the college, announced. Dr. North, who will succeed Dr. Paul R. Hawley, Chicago, the college's director since March, 1950, has been chief, Surgical Service, Veterans Hospital, Dallas, since 1955, and professor of clinical surgery at Southwestern Medical School of the University of Texas since 1946. He has been a fellow of the college since 1935 and a member of the board of governors since 1954.

New Fifty Year Club.—Dr. John H. McCurry, of Cash, Ark., is interested in forming an A. M. A. Fifty Year Club in which membership would be limited to members of the Association who have been in practice 50 years or more. The first meeting of the new club is expected to be held during the annual clinical meeting of the Association in Washington, D. C., in November, 1960. Those who are qualified and desire to join this organization are requested to so advise Dr. McCurry, giving their complete name and address. Dr. McCurry plans to be in Miami at the June meeting to begin organizational procedures and to see any who qualify at this meeting.

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Cross Examination of the Medical Witness, Mr. Albert Auerback, Seneca Falls.

The Back in Diagnosis and Litigation, Drs. Harold Lefkoe, Philadelphia, and Jacob Urdang, Brooklyn.
Medical Evidence of Disability Under the Social Security Administration, Dr. Joseph Lerner, Ijamsville, Md.
Analysis of Recent Medico-Legal Cases, Dr. Alfred Koerner, New York City.

Registration fee for nonmembers at the Philadelphia meeting is $7.50 (including luncheon). For information, write Dr. Harold Lefkow, Secretary, 1003-06 Medical Tower, Philadelphia 3.

Postgraduate Assembly in Memphis.—The 71st annual meeting of the Mid-South Medical Assembly will be held Feb. 9-12 in Memphis, Tenn., sponsored by the Memphis Academy of General Practice and Tennessee Academy of General Practice. The program includes 19 guest speakers:

Drs. John A. Wall Jr., Houston, Texas; Alan J. Johnson, Frank E. Stinchfield, Horace L. Hodes, and Herbert Conway, New York City; Thomas F. Paine Jr., Birmingham; Col. Paul A. Campbell, Brooks Air Force Base, Texas; J. Robert Willson, Philadelphia; Jack S. Guyton and John R. McDonald, Detroit; Lester A. Brown, Atlanta; Harry Medovy, Winnipeg, Canada; John A. Campbell, Indianapolis; Samuel F. Marshall and Donald Matson, Boston; Richard T. Shackelford, Baltimore; Earle B. Kay, Cleveland; John E. Heslin, Albany, N. Y.; and William F. Miller, Dallas.

A clinical pathological conference, symposiums, and exhibits are planned. The assembly has been approved for category I by the A. A. G. P. Registration fee is $20, and reservations should be addressed to the Hotel Reservations Committee, 774 Adams Ave., Memphis 5, Tenn.

Abdominal Surgeons Meeting.—The Clinical Congress of Abdominal Surgeons will be held in Miami Beach, Fla., Feb. 1-5. The scientific program consists of panel discussions on the following subjects:

Pre- and Postoperative Care.
Intestinal Obstruction.
Diverticulitis.
Surgery of Gastric and Duodenal Ulcer.
Present Status of Diagnosis and Treatment of Stomach Cancer.
Hernia.
Biliary Tract Surgery.
Surgery of the Rectum and Colon.
Indications for Hysterectomy.
Surgery of Pelvic Cancer.
What's New in Abdominal Surgery.

There will be a film program conducted throughout the week. A special panel on malpractice will be moderated by Judge Felix Forte, of the Massachusetts Superior Court. A program of entertainment is planned. For information, write Dr. Blaise F. Alfano, 663 Main-St., Melrose 76, Mass., Boston, P. O.

Conference on Biological Waste Treatment.—Forty-five technical papers, including 10 from the countries of England, Germany, Holland, Japan, and Sweden, will be delivered at the third Conference on Biological Waste Treatment at Manhattan College, New York City, April 20-22. Devoted to new advances in biological oxidation and oxygen transfer in the disposal of waste from industry and municipalities, the conference is international in scope and is made possible by a grant from the Department of Health, Education, and Welfare. Conference chairman is W. Wesley Eckenfelder, associate professor of civil engineering at Manhattan. The program will be divided into four categories: theory of biooxidation, recent advances in biological oxidation, oxygen transfer theory and developments, and biooxidation of sewage and industrial wastes. There will be two simultaneous sessions with scheduled discussion periods after each session. Preregistration will be necessary. Interested participants should contact Professor Eckenfelder at Manhattan College, New York 71.

Surgeons Meeting in Colorado Springs.—A three-day sectional meeting of the American College of Surgeons will be held in Colorado Springs, Colo., March 21-23, with headquarters at the Broadmoor Hotel. The program will include scientific reports on topics of current concern such as management of the injured hand, treatment of duodenal ulcer, appendicitis, treatment of neck fractures, surgical convalescence, and cancer and pregnancy. Symposiums on injuries, cancer, and hospital infections will be presented. Medical motion pictures and clinic films from the 1959 clinical congress will be shown. Panel discussions are planned on parenteral therapy and upper gastrointestinal tract hemorrhage. Wednesday, March 23, Dr. Paul R. Hawley, Chicago, the director of the college, will be the speaker at the dinner. The subject of his talk will be "The Epidemiology of An American Legend." Dr. H. Prather Saunders, associate director, the American College of Surgeons, 40 E. Erie St., Chicago 11, is in charge of all sectional meetings for the college.

Foreign Physicians Receive Fellowships.—The World Rehabilitation Fund announced the awarding of five fellowships to physicians from Brazil, Yugoslavia, India, and Colombia for advanced training in physical medicine and rehabilitation in the United States. The fellowships are for a period of one year but subject to renewal. All of the recipients began their training on Jan. 1 in the department of physical medicine and rehabilitation, New York University Bellevue Medical Center. The fellowship recipients include: Dr. Vera Maric, Belgrade, Yugoslavia; Dr. Marino Quintero, Cali, Colombia; Dr. Miguel Rangel, Bogota, Colombia; Dr. Mary Verghese, Christian Medical College, Vallore, South India; and Dr. Haroldo Campos Guimaraes, Pfizer Fellow in Rehabilitation, Sao Paulo, Brazil. The new fellowships bring the total number of trainees who are receiving long-term advanced training in the U. S. under the auspices of the World Rehabilitation Fund during the current academic year to 66 trainees (41 physicians and 25 nonphysicians) for 36 different nations. The World Rehabilitation Fund is a nonprofit organization supported by American industry, foundations, and individuals to assist in the international development of rehabilitation services for the physically handicapped.

Decline in Hospital Construction.—The American Association of Fund Raising Counsel, Inc., reported a decline in private hospital construction during 1959. New private hospital construction for the first nine months of 1959 was valued at $425 million, a 7% decline over the 1958 comparable figures, according to the AAFRC. About 150 million dollars of the expenditure for new construction came in current philanthrophy. The average daily census in hospitals increased by 4.5 million, to a total of 26.5 million. The capital needs of hospitals are estimated at 500 million dollars a year for the next 20 years. Disparity between patient charges and hospital costs is shown by the fact that in 1957, patient care cost about $.95 while the same patient in 1958 cost the hospital about $1.52, an increase of 62%. In spite of the 7,000 hospitals in the United States at the start of the 1958-1959 fiscal year, government sources have estimated total need of 864,236 new beds and replacement of 280,273 beds which are in use but below minimum standards. Cost of a bed today is reported to be more than double the $11,987 price in 1948. The American Association of Fund-Raising Counsel, Inc., is a nonprofit organization of 31 professional firms specializing in directing, counseling, and organizing fund-raising activities in the United States and Canada.

Rehabilitation Fellowships for Foreign Physicians.—The creation of six Reader's Digest Foundation fellowships in rehabilitation for advanced training in the United States for physicians from France, Italy, Spain, Mexico, Japan, and Brazil, was announced Dec. 17 by Dr. Howard A. Rusk, New York City, president of the World Rehabilitation Fund. The six fellowships are being created by the fund with a contribution from the Reader's Digest Foundation. The fellowship for the physician from Italy is named the Gian Pietro Giordana Memorial Fellowship in memory of the late managing director of the Italian edition of the *Reader's Digest* who died June 26. Simultaneous announcement of the six fellowships was made in France, Italy, Spain, Japan, Mexico, and Brazil by the ambassadors of the United States to each of these nations. The recipients of the fellowships will be provided with a minimum of one year of postgraduate training at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center. The fellowships will provide tuition and a tax-exempt stipend of $250 per month or its equivalent. Information concerning the fellowships can be secured from the World Rehabilitation Fund, Inc., 400 E. 34th St., New York 16. The fellowships are being awarded by the World Rehabilitation Fund in cooperation with the International Society for the Welfare of Cripples and its affiliates or representatives in the six nations.

Orthopsychiatric Meeting in Chicago.—The 37th annual meeting of the American Orthopsychiatric Association will be held Feb. 25-27 at the Sherman Hotel, Chicago. Psychiatrists, psychologists, psychiatric social workers, and educators as well as interested laymen will attend scientific sessions and workshops on currently important topics, including problems of adolescence, childhood psychoses, brain damage, the impact of segregation on child development, adult therapy, and proposed legislative measures related to juvenile delinquency. Registration is open to nonmembers. The association is a national professional organization which brings together the disciplines involved in the team approach to prevention and treatment of behavior problems and related training and research. According to Marion F. Langer, Ph.D., executive secretary of the association, the program will include joint sessions with the American Public Health Association, the World Federation of Mental Health, the American Group Psychotherapy Association, the Society for Projective Techniques, the American College Health Association, and the American Association of Psychiatric Clinics for Children. In his presidential address, Walter M. Mathews, Ph.D., psychologist at the Merrill–Palmer School, Detroit, will speak on healthy child development. More than 40 workshops and 70 scientific papers are scheduled. Information is available from Dr. Langer, 1790 Broadway, New York 19.

FOREIGN

Physician Sentenced for Private Practice in Prague.—Dr. Dostal, a physician in Prague, has been sentenced to 18 months in prison for unauthorized practicing in a private office, the newspaper *Heimatruf*, published in Munich, reported Nov. 21. This paper replaced the paper of the Germans in the Sudetic Mountains in Northwestern Czechoslovakia.

Clinical Pathology Meeting in Madrid.—The fourth International Congress of Clinical Pathology will be held in Madrid, Spain, June 7-13. Official languages will be Spanish, English, and French, with simultaneous translations available. Six general subjects are specified for discussion in special sessions as follows:

Recent Advances in Immunohematology.
Enzymes in Histopathologic Laboratory Diagnosis.
Tissue Culture in Bacteriological Virologic and Parasitological Diagnosis.

Evaluation of Hormones and Their Application to Diagnosis.
Differential Diagnosis in the Icteric Patient.
Biopsy of Organs in Clinical Diagnosis.

A meeting on forensic pathology is planned with the following topics: unknown causes of death with minimum visible lesions, toxicologic investigation in cadaver blood, and accidents in sanguineous transfusion. A symposium on pathology of some systematized bone diseases has been arranged to take place in Barcelona prior to the congress. Registration fee for ordinary members is $25 and for associate members (persons accompanying ordinary members), $12.50. A ladies' program is arranged. For information, write the Secretary General, Fourth International Congress of Clinical Pathology, Pabellon 11 de la Facultad de Medicina, Ciudad Universitaria, Madrid, España.

Cardiology Congress in Australia.—The second Asian-Pacific Congress of Cardiology will meet in Melbourne, Australia, May 30-June 3, with the cardiac Society of Australia and New Zealand acting as host. The scientific program will be held at the University of Melbourne. The Royal Australian College of Physicians will hold their annual meeting during the preceding week. The following subjects have been chosen as the basis for round-table discussions and symposiums:

- Open Heart Surgery.
- Coronary, Cerebral and Peripheral Arterial Disease.
- Physiological Studies.
  - Mechanisms of Heart Action
  - Metabolism of Heart Muscle
- Therapeutics.
  - Hypertension
  - Cardiac Failure
- Instrumental Diagnostic Methods.
  - Electrocardiography
  - Radiography
  - Other Recording Methods
- General.
  - Rheumatic Heart Disease
  - Hypertension and Renal Disease
  - Congenital Anomalies
  - Heart Disease of Obscure Origin

Full membership is open to all members of the medical profession and to scientific and research workers interested in cardiology. Fees are £A15 ($33.75) for full membership and £A10 ($22.50) for associate membership (wives and adult children). A scientific exhibition and a trades' exhibition are planned. The congress banquet will be held the evening of June 2. For information, write Dr. A. E. Doyle, Alfred Hospital, Melbourne, S. 1, Victoria, Australia.

CORRECTION

Therapeutic Experience with Triamcinolone in Acute Viral Hepatitis.—In the abstract entitled "Therapeutic Experience with Triamcinolone in Acute Viral Hepatitis," The Journal, Dec. 5, 1959, page 2026, the dosage should have been 0.30 mg. and not 3 mg.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 19-20. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Connecticut:* *Regular. Examination.* Hartford, Mar. 8-10. Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven. *Homeopathic. Examination.* Derby, Mar. 8. Sec., Dr. Ronald A. Davis, 38 Elizabeth St., Dover.

Georgia: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act Sec., Dr. F. L. Conklin, Agana.

Indiana: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Mississippi: *Examination.* Jackson, June. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

Montana: *Examination and Reciprocity.* Helena, April 5. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

New Hampshire: *Examination.* Concord, March 9-11. *Reciprocity.* Concord, March 9. Sec., Dr. Edward W. Colby, 61 South State St., Concord.

Oklahoma:* *Examination.* Oklahoma City, May 31-June 1. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Utah: *Examination.* Salt Lake City, July 6-8. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

Wyoming: *Examination and Reciprocity.* Cheyenne, Feb. 1. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arkansas: *Examination.* Little Rock, April 21-22. Sec., Dr. A. W. Ford, Department of Education, Education Bldg., Little Rock.

Colorado: *Examination and Reciprocity.* Denver, March 2-3. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, Feb. 13. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

Kansas: *Examination.* Kansas City, June 10-12. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburgh.

Michigan: *Examination.* Detroit and Ann Arbor, Feb. 12-13. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Oklahoma: *Examination.* Oklahoma City, April 15-16. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Texas: *Examination.* Austin, Houston, Galveston and possibly Dallas, April 15-16. Sec., Dr. Cornelia M. Smith, State Office Bldg., 201 East 14th St., Austin.

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*Basic Science Certificate required.

DEATHS

Cotton, James Oliver Ⓜ North Little Rock, Ark.; born Dec. 30, 1872; Barnes Medical College, St. Louis, 1899; for many years practiced in Leslie, Ark., where he founded the first drug store and was city treasurer; past-president of the Searcy County Medical Association; died in Little Rock Oct. 12, aged 86.

Curtis, Mildred Ⓜ Iola, Kan.; University of Kansas School of Medicine, Lawrence–Kansas City, 1906; on the staff of Allen County Hospital; died in Mercy Hospital, Fort Scott, Oct. 4, aged 79.

Dabney, Thomas Gregory, Berkeley, Calif.; University of Virginia School of Medicine, Charlottesville, 1901; also a pharmacist; at one time medical director of the Equitable Life Assurance Society; died at the Peralta Hospital, Oakland, Oct. 7, aged 84.

de Savitsch, Eugene Constantine, London, England; born in Petrograd, Russia; University of Chicago, the School of Medicine, 1935; at various times practiced in France, Belgium, the Belgian Congo, and Washington, D. C.; at one time a research fellow in physiology at his alma mater; member of the International College of Surgeons, the American College of Chest Physicians, American Trudeau Society, and American Society for Experimental Pathology; at one time on the staff of Doctors Hospital, Washington, D. C.; died Oct. 15, aged 56.

Drake, James Carl, Fresno, Calif.; Washington University School of Medicine, St. Louis, 1911; interned at St. Louis City Hospital; at one time practiced in St. Louis; served with the 35th Division of the U. S. Army during World War I; physician in charge of the well baby clinics of Fresno County; on the staffs of St. Agnes and Community hospitals; died Oct. 7, aged 76.

Fechter, Francis Robert Ⓜ Milwaukee; Marquette University School of Medicine, Milwaukee, 1941; interned at St. Joseph's Hospital; died Oct. 9, aged 45.

Gibson, Frank James Ⓜ St. Petersburg, Fla.; University of Michigan Medical School, Ann Arbor, 1902; for many years practiced in Jackson, Mich., where he served as chief of staff at Foote and Mercy hospitals; died Oct. 5, aged 84.

Goodwin, Thomas Martin Ⓜ Elkins, W. Va.; New York University College of Medicine, New York City, 1929; interned at St. Luke's Hospital, Newburgh, N. Y.; served residencies at the Baltimore (Md.) Eye, Ear, and Throat Charity Hospital and Brooklyn (N. Y.) Eye and Ear Hospital; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Oto-Laryngology, American Society of Ophthalmologic and Otolaryngologic Allergy, and International College of Surgeons; served as a surgeon in the U. S. Public Health Service during World War II; a founder of the Golden Clinic and Memorial General Hospital; died in Chicago Oct. 17, aged 54.

Gosney, Charles William, Los Angeles; St. Louis (Mo.) College of Physicians and Surgeons, 1900; for many years practiced in Kansas City, Mo.; member of the American Academy of Ophthalmology and Oto-Laryngology; on the staffs of Cedars of Lebanon Hospital and Hollywood Presbyterian Hospital, where he died Oct. 10, aged 85.

Graff, Elfie Richards, Gulfport, Fla.; born in Cincinnati March 22, 1875; Woman's Medical College of Pennsylvania, Philadelphia, 1905; for a time practiced in Somerville, N. J., after which she became a medical missionary in Turkey; later helped found a sanitarium in Russian Armenia and the American Woman's Hospital in Greece; public health worker in Pennsylvania, Kentucky, and New York; member of the American Association of University Women; died Oct. 14 in Cedars Hospital, aged 84.

Gratzek, Thomas Ⓜ St. Paul, Minn.; University of Illinois College of Medicine, Chicago, 1911; interned at Cook County Hospital, Chicago; fellow of the American College of Surgeons; served with the Army Medical Corps during World War I; a founder of the St. Paul Polish–American Club; at one time Ramsey county deputy coroner; on the staff of St. John's Hospital; died in Harding, Minn., Oct. 9, aged 74.

Graves, Alexander Wilson, Gadsden, Ala.; Medical College of Alabama, Birmingham, 1916; served during World War I; died in Dadeville, Ala., Oct. 6, aged 67.

Griffith, Daniel Moseley Ⓜ Owensboro, Ky.; born in Owensboro on Sept. 19, 1867; Tulane University School of Medicine, New Orleans, 1888; fellow of the American College of Surgeons; was elected to two consecutive terms as president of the Kentucky State Medical Association; member of the A. M. A. House of Delegates in 1920; in 1953 received an award for distinguished and outstanding service

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Ⓜ Indicates Member of the American Medical Association.

to the profession at the first World Medical Conference at Richmond, Va.; was a co-organizer and past-president of the Ohio Valley Medical Society; one of five physicians selected by President Woodrow Wilson during World War I to organize the medical profession for service in that conflict; member of the City Council and trustee of the library; associate organizer and vice-president of the Owensboro Training School for Nurses; on the staffs of Owensboro Daviess County and Mercy hospitals; died Oct. 9, aged 92.

Haley, Philip Stephen Ⓜ San Jose, Calif.; St. Louis University School of Medicine, 1929; interned at St. Mary's Hospital, San Francisco; served a residency at the San Jose (Calif.) Hospital; during World War II served as a lieutenant commander in the Navy Medical Corps, and won a presidential citation for bravery for his part in the rescue of survivors of the carrier Wasp off Guadalcanal; member of the American Academy of General Practice; on the staffs of O'Connor Hospital and San Jose Hospital, where he died Oct. 11, aged 58.

Harbridge, Delamere Forest Ⓜ Phoenix, Ariz.; born in Racine, Wis., June 18, 1872; University of Pennsylvania School of Medicine, Philadelphia, 1898; member of the A. M. A. House of Delegates in 1921; specialist certified by the American Board of Ophthalmology; former secretary and president of the Arizona Medical Association; past-president of the Maricopa County Medical Society; member of the American Ophthalmological Society and the American College of Surgeons; at one time secretary-treasurer of the board of managers of *Southwestern Medicine;* died in Los Angeles Oct. 6, aged 87.

Heffner, George W., Columbus, Ohio; Starling Medical College, Columbus, 1895; for many years practiced in Circleville, Ohio; served as Pickaway County health officer; died in Lankenau Hospital, Philadelphia, Oct. 7, aged 88.

Heimbach, James Michael, Kane, Pa.; born in Herford Township, Berks County, Pa., Dec. 14, 1869; Hahnemann Medical College and Hospital of Philadelphia, 1897; president of the Homeopathic Medical Society of Pennsylvania in 1916; in 1927 named president of the National Society of Physical Therapy and associate of the American Institute of Homeopathy; member of the International Hahnemannian Association, American Association for Medico-Physical Research, National Proctologic Association, Institute of Metaphysics, Pelman Institute of America, and the American Association for the Advancement of Science; served for six years on the board of education; died Oct. 2, aged 89.

Irons, Frank Ernest Ⓜ Winter Haven, Fla.; University College of Medicine, Richmond, Va., 1905; past-president of the Polk County Medical Society; honorary member of the staff of Winter Haven Hospital; died Oct. 6, aged 81.

Kelly, Virgil Leonidas Ⓜ Bluefield, W. Va.; University of Virginia School of Medicine, Charlottesville, 1928; interned at the Blue Ridge Sanatorium, Sanatorium, Va., and the University of Virginia Hospital; member of the American College of Chest Physicians and the American Trudeau Society; past-president of the Green Valley Kiwanis Club; on the staff of Bluefield Sanatarium; died Oct. 10, aged 55.

Kennedy, Edward La Tane, Smithland, Ky.; University of Tennessee College of Medicine, Memphis, 1900; at one time practiced in Greenfield, Tenn., and later in Green County, Ark., and Milburn and Tiline, Ky.; in April was honored by a special community program; died Oct. 6, aged 83.

Krohn, Harry Nathaniel, Los Angeles; born in Russia in 1880; University Medical College of Kansas City, Mo., 1904; served as a major during World War II with the Army Medical Corps; on the staff of Cedars of Lebanon Hospital; died Oct. 14, aged 79.

McAuliffe, Joseph Patrick, Chicago; Stritch School of Medicine of Loyola University, Chicago, 1918; interned at the Hospital of St. Anthony de Padua, Chicago; died in Alexian Brothers Hospital Oct. 19, aged 74.

McCarthy, Patrick A. Ⓜ Philadelphia; Jefferson Medical College of Philadelphia, 1908; associate professor of surgery at his alma mater; a founder of the American Board of Surgery; fellow of the American College of Surgeons; member of the Medical Club of Philadelphia; on the staffs of Philadelphia General Hospital, where he was chief of surgical service, and Jefferson Medical College Hospital, Germantown Hospital, and St. Mary's Hospital, where he was director of surgery and where he died Oct. 23, aged 75.

McCollum, Charles Holmes, Jr. Ⓜ Forth Worth, Texas; Tulane University School of Medicine, New Orleans, 1933; interned at the City and County Hospital, Fort Worth, where he also served a residency; president and director of the Junior Chamber of Commerce and received the distinguished service award of the Fort Worth Junior Chamber of Commerce in 1941; in 1940 was named Fort Worth's outstanding young man of the year; served during World War II as a lieutenant commander in the Navy; member of the board of the Fort Worth Housing Authority; at one time chairman of the St. Joseph Hospital staff; died Oct. 5, aged 52.

McIntire, Ross T. Ⓜ Chicago; vice-admiral, U. S. Navy, retired; former surgeon general of the Navy; Willamette University, Medical Department, Salem, Ore., 1912; interned at Salem (Ore.) Hospital; specialist certified by the American Board of Otolaryngology; began practice in Oregon; in 1917 became a lieutenant commander in the Navy Medical Corps; became chief of the Bureau of Medicine and Surgery in 1938; during his military career served in World Wars I and II, in various naval hospitals, in the Philippines, and aboard the USS New Orleans and the hospital ship Relief; served as instructor in ophthalmology and otolaryngology in the Naval Hospital, Washington, D. C.; at one time head of the eye, ear, nose, and throat department of the Naval Hospital, San Diego, Calif.; personal physician to President Franklin D. Roosevelt; since 1955 executive director of the International College of Surgeons; served as director of the American Red Cross National Blood Bank Program and as chairman of the President's Committee on National Employ the Handicapped Week; awarded the Navy's Distinguished Service Medal, the World War I Victory Medal with Escort Clasp, the American Defense Medal with Bronze Star, the American Campaign Medal, the World War II Victory Medal, the U. S. Typhus Commission Medal, and received various decorations and awards from the countries of Brazil, Sweden, Belgium, France, Luxembourg, Denmark, Poland, Nicaragua, Norway, and French Morocco; at one time on the advisory board of the Society for the Prevention of Asphyxial Death; member on the National Board of Medical Examiners; on the board of directors of the American Foundation for Tropical Medicine and the board of governors of the American College of Surgeons; trustee of the Georgia Warm Springs Foundation; member of the Health Committee of the National Research Council and the Association of Military Surgeons; from August, 1942, to June, 1946, a member of the United States of America Typhus Commission; honorary fellow of the American Surgical Association and the American College of Surgeons; in 1955 gave the Collier Ford Martin Oration of the the Philadelphia Proctologic Society; received the honorary degree of doctor of science from Marquette University School of Medicine, Milwaukee, in 1943; died in Grant Hospital Dec. 7, aged 70.

McKeever, Duncan Clark Ⓜ Houston, Texas; University of Kansas School of Medicine, Lawrence–Kansas City, 1929; interned at the U. S. Naval Hospital, Brooklyn, and St. Luke's Hospital, Kansas City, Mo.; specialist certified by the American Board of Orthopaedic Surgery; past-president of the American Fracture Association and the Association of Bone and Joint Surgery; vice-president of the Houston Society of Clinical Hypnosis and the Texas Orthopedic Association; fellow of the American College of Surgeons; member of the Clinical Orthopaedic Society and the American Academy of Orthopaedic Surgeons; served in the Navy Medical Corps during World War II; chief orthopedic surgeon at the Baptist Memorial Hospital, where he had been president of the staff in 1957 and where he died Oct. 13, aged 54.

Matuska, Ignatius Wenceslaus Ⓜ Cleveland; Western Reserve University School of Medicine, Cleveland, 1914; interned at St. Alexis Hospital, where he was on the staff and where he died Oct. 2, aged 71.

Miller, Harold Albert Ⓜ Saline, Mich.; University of Michigan Medical School, Ann Arbor, 1935; interned at Harper Hospital, Detroit; served with the U. S. Army Medical Corps in the South Pacific; member of the Saline Board of Education for eleven years and president for four years; president of the Saline Hospital Association; member of the American Academy of General Practice and the Aero Medical Association; vice-chief of staff of Saline Hospital and on the staffs of St. Joseph Mercy Hospital, Ann Arbor, and Beyer Memorial Hospital, Ypsilanti; died Oct. 15, aged 48.

Moore, Samuel Aloysius Ⓜ Daytona Beach, Fla.; University of Buffalo School of Medicine, 1904; practiced in Buffalo for many years; member of Phi Rho Sigma; died in Halifax District Hospital Oct. 12, aged 79.

Mosby, Charles Porter Ⓜ Meridian, Miss.; Hospital College of Medicine, Louisville, Ky., 1904; served during World War I; died Oct. 9, aged 84.

O'Dea, Nellie Geraldine, Scranton, Pa.; Temple University School of Medicine, Philadelphia, 1915; interned at Allentown (Pa.) Hospital; died Oct. 3, aged 73.

Parman, David Robert, St. Louis; St. Louis University School of Medicine, 1903; formerly on the faculty of Washington University and on the staff of Missouri Baptist Hospital; died Oct. 3, aged 83.

Roy, Frank Keller, Kansas City, Mo.; born in Palmyra, Mo., in 1871; University Medical College of Kansas City, 1900; practiced in Clarence for many years; died Oct. 13, aged 88.

Shirley, Amos Reginald Ⓜ Wauwatosa, Wis.; University of Vermont College of Medicine, Burlington, 1915; veteran of World Wars I and II; member of the Roentgen Ray Society; chief of radiology at the Veterans Administration Regional Office, from which he retired in 1955; held posts with the War Risk Insurance Bureau, the U. S. Public Health Service, and the Veterans Administration Center in Wood; past-state commander of the Military Order of World Wars; died Oct. 16, aged 72.

FOREIGN LETTERS

FRANCE

Griseofulvin.—Sidi and Spinasse (*Press méd.*, May 30, 1959) used griseofulvin in the treatment of a series of 20 patients who had the most stubborn type of mycoses. For the adult patients 1 to 1.5 Gm. was given daily by mouth. From the third week after the start of the therapy the authors noticed a definite improvement from the lunula to the end of the nail. In a patient with onychomycosis of three years' duration, but whose nail lesions had started at different times, a nail that had been deformed for six months was completely cured after two months' treatment, and in the nails with older lesions the lunula had also recovered. The results of mycotic examinations become negative only after the distal part of the nail was cured, and the onychomycosis caused by Trichophyton rubrum responded faster than other types to this treatment.

Trichophyton tonsurans was isolated in a 2½-year-old child with tinea capitis of three months' duration and consisting of several plaques disseminated over the scalp. One of these plaques measured 5 by 6 cm. and was particularly fluorescent. The child received at first 375 mg. of griseofulvin daily, then 500 mg. a day for 15 days. At the end of two weeks all recent plaques and the fluorescence had disappeared, and the results of the examination had become negative. Six weeks later all lesions were completely cured and hair had grown over the diseased areas. The treatment was continued for another two weeks with a daily dose of 250 mg. One month after completion of the therapy there had been no relapse. In two patients with generalized pityriasis versicolor, griseofulvin was ineffective, but the patient with erythrasma showed definite improvement after a 15 days' treatment with a daily dose of 1.5 Gm. and without any local treatment.

A dramatic cure was obtained in four patients with dyshidrosis and lesions of five to seven years duration. These lesions became dry and disappeared within eight days in one patient and within three weeks in the other. Their skin became smooth and normal, and there was no recurrence within several weeks after the therapeutic period. In two other patients, however, there was a sudden, violent, and extensive aggravation of the lesions, extending even to the feet, which had been spared until then. Before the treatment a mycotic examination on this patient had revealed a Penicillium glaucum which was difficult to classify as either saprophytic or pathogenic.

In order to study the possible effect of intersensitization between penicillin and griseofulvin, epicutaneous tests and scarifications with griseofulvin were given to six patients whose skin tests had shown violent reaction to penicillin and who had suffered serious accidents after an intramuscular injection of this antibiotic. The results of the griseofulvin tests were negative, and the oral administration of a daily dose of 250 mg. to three of the patients and of 1 Gm. to another for two days did not cause any allergic reaction. There was perfect tolerance to griseofulvin. No changes were observed in the blood chemistry. The daily doses used by the authors were 1.0 to 1.5 Gm. for adults and 500 to 750 mg. for children, whereas William and co-workers and H. Blank used larger doses.

Oxytetracycline Perfusion.—H. Thiers and co-workers (*J. méd. Lyon*, June 20, 1959) treated 171 patients who had ulcerations, torpid or gangrenous wounds of the lower extremities, generalized infected eczema, pyodermatitis, epithelioma, erythroderma, and osteomyelitis with perfusions of oxytetracycline in an isotonic sodium chloride or dextrose solution. The average dosage of the antibiotic was 750 mg. In those with severe infection the perfusions were given daily for six days, then every second or third day until 15 perfusions had been given. Some mild digestive reactions were observed, which led to interruption of the treatment in eight patients. No hematological changes resulted from prolonged treatment. The results were satisfactory. For torpid wounds and gangrene from arteritis, the treatment had to be prolonged. This therapy was an excellent preparation for operation. Patients with severe bacterial eczema and with osteomyelitis showed improvement after 6 to 12 perfusions. Excellent results were obtained in those with erythroderma and ulcerative pyodermatitis.

Angina Pectoris.—R. Gérard and co-workers (*Presse méd.*, May 13, 1959) treated a series of 25 patients who had angina pectoris, resistant to the usual medicaments, with intradermal injections of a preparation containing 75 mg. of monoethanolamine-nicotinate and 50 mg. of heparin. The injections were made every three or four days in selected painful spots. These spots included the region of the scapulohumeral articulation and various points of referred pain. In 7 of 10 patients who had angina pectoris associated with scapulohumeral periarthritis, or with a cervical arthrosis, the pain disappeared, in 2 there was partial improvement, and in 1 there was no relief. Of six patients with coronary angina

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The items in these letters are contributed by regular correspondents in the various foreign countries.

without articular involvement, the pain disappeared completely in five and one had only slight relief. In nine patients who continued to have pain on exercise and at rest after a myocardial infarction, the treatment resulted in prompt relief of the pain but was ineffective when repeated. The authors emphasized the fact that only the association of the vasodilator with the anticoagulant was effective; separately, the two substances gave no relief. The treatment reported is simple and safe and should be used whenever all other treatment fails.

Polymyxin for Gastroenteritis.—J. Fleury and R. Evreux (*Nourrisson*, no. 2, 1959), during three epidemic outbreaks in 1957, treated a series of 77 children who had gastroenteritis, mostly due to Escherichia coli O III B4, already strongly resistant to antibiotics. They gave 25 mg. of polymyxin daily. Vomiting stopped in two to four days, diarrhea in less than three days, and dehydration within 24 hours. Complete recovery was observed in 73 patients, including some whose infection was most severe. Only 3 (3.5%) died, in contrast with 11 (16%) in a control group of 70 patients who were treated with other antibiotics. Only five in the control group were cured. With their large experience the authors became able to establish a clinical diagnosis based on the presence of anorexia, vomiting, sudden loss of weight, excessive dehydration, and diarrhea with pale yellow feces mixed with whitish mucus and with a stale odor. Without waiting for a confirmation by culture of the feces, the authors started treatment with polymyxin at once. A daily prophylactic dose of 25 mg. of the drug was also given to all infants entering the hospital. As a result these infants were kept healthy in the midst of an epidemic which was thus promptly controlled.

GERMANY

Prednisolone for Pulmonary Tuberculosis.—U. Baldamus and E. G. Ewert (*Deutsche med. Wchnschr.* 84:1625, 1959) reported treatment of 85 patients who had extensive, cavernous, pulmonary tuberculosis. Prednisolone was given for an average of three months, in addition to the usual forms of chemotherapy. The initial dose was 20 mg. daily, followed by a maintenance dose of 5 to 10 mg. Indications for its use included (1) hematogenous, bilateral pulmonary tuberculosis with high fever in patients having had no previous chemotherapy; (2) therapy-resistant, extensive, predominantly infiltrative cavernous pulmonary tuberculosis; and (3) tuberculous pleuritis. In 67% of the patients there was a definite prednisolone effect, which could be distinguished from the effects of specific chemotherapy. Prednisolone was most effective in the hyperergic toxic forms of tuberculosis. There was no evidence that the bacterial resistance to antituberculosis drugs was influenced by the hormone. In six patients prednisolone treatment made operation possible. There were no undesirable side-effects. There was a remarkable lack of prednisolone effect in patients who had conditions other than pulmonary tuberculosis.

Maternal Mortality.—According to a report (*Deutsche med. Wchnschr.* 84:1662, 1959) the high maternal death rate in the federal republic in 1955 led to a reappraisal of the concept of maternal deaths. The fall in this rate from 157 per 100,000 live births in 1955 to 139 in 1956 was probably representative less of a true reduction accomplished by prophylactic and therapeutic measures than of a new, more accurate, conception of the term "maternal mortality." Moreover, this fall was based on the reduction in the number of deaths from complications of pregnancy, labor, and the puerperium. Under this heading many deaths which were due to such primary causes as heart disease, and thus should not be regarded as genuine maternal deaths, were undoubtedly included up to 1955. In 1957 the rate was further reduced to 128. The death rate from toxemias of pregnancy, puerperal toxicoses, and postpartum hemorrhage remains high in comparison with that of other countries.

Meconium Peritonitis.—Rehbein and Wolfrom of Bremen (*Chirurg* 30:15-19, 1959) added 2 cases of meconium peritonitis to the list of 22 cures described in the literature between 1943 and 1957. In the first patient an obvious swelling bigger than a man's fist was present in the scrotum at birth. This was greenish in color and shiny. At operation air and greenish fluid were released. The whole of the inner surface of the scrotum, as well as the peritoneum of the rectovesical pouch and the right lower abdominal quadrant were filled with masses of a green substance. No perforation was found in either the ileum or the colon. In the other patient there was a diaphragmatic hernia on the right, and the infant's general condition was poor at birth. The scrotum was enlarged and had a greenish discoloration. Although the intestines were intact throughout, the peritoneum was saturated with meconium.

In 50% of such patients there is evidence of congenital atresia, which gives rise to congestion, dilation, ischemic necrosis, and perforation. In the rest the cause is not so obvious. Various theories have been advanced: hypertrophy of lymphatic tissue with pressure atrophy of the muscularis mucosae, mucosal ulceration, congenital lacunae in the intestinal wall, cystic fibrosis of the pancreas, more rarely a Meckel's diverticulum of the appendix, or abnormal enlargement of the points of entry of the blood vessels through the muscularis. X-ray examination, with demonstration of pneumoperitoneum and fluid levels, which are associated with recent perforation, should never be omitted. Operation is the only treatment, and the prognosis, if the condition is recognized promptly, is no longer gloomy.

Infections in Infancy.—E. Klein of Göppingen (*Medizinische*, pp. 282-285, 1959) used tetracycline in the treatment of 140 infants who had infections. The dosage varied between 10 and 125 mg. per kilogram of body weight per day, with an average of 125 mg. Cure was achieved in 101, or 72%. Side-effects were few and slight, the most noteworthy being the appearance of a severe enteritis in six of the infants. A precise bacteriological diagnosis could not be arrived at, but no staphylococci were demonstrated. The author emphasized the necessity for rational therapy with establishment of the sensitivity of the causative organisms and stressed the importance of supportive measures in addition to antibiotic therapy.

Treatment of Nephroses.—Acker and Schreier of Heidelberg (*München. med. Wchnschr.* 101:221-224, 1959) since 1945 treated a series of 55 children who had nephroses; 22 were treated without and 33 with glucocorticoids or ACTH. Comparison of the results of treatment is difficult, if not impossible, because the follow-up period in the children treated with hormones was much shorter than that in the others, and a permanent cure cannot be assumed after an observation period of less than five years.

A low-fat, high-protein, salt-poor diet is still an essential part of the treatment. Diuretics are of doubtful value. Surgical procedures such as paracentesis or renal decapsulation did not produce any lasting effect. Although tolerance of thyroid extract was high in all patients tested, no importance could be attributed to this method of treatment. Administration of glucocorticoids produced a clinical cure in six patients. The total provisional cure rate was 75%. In patients who had nephrosis with a nephritic element the cure rate was even better. In the previous 10 years 50% of the patients died, while the prognosis for the remainder was doubtful. Whereas most children with nephroses formerly died of intercurrent infections, no more deaths have resulted since adequate supplies of antibiotics have been available.

Poliomyelitis.—M. Hertl of Heidelberg (*Medizinische*, pp. 410-414, 1959) subdivided the variegated and protean picture which poliomyelitis presents into (1) a meningeal form without any neurological deficit but with patchy involvement of hypothalamic nuclei, giving rise to autonomic disturbances such as fever, sleep disturbances, sweating, and constipation; (2) a purely spinal form with reflexes absent and pareses or paralysis in the gluteal region; (3) a spinal form with involvement of the accessory nerve, leading to paralyses of the limbs and gluteal muscles and pareses of the neck and shoulder muscles; (4) a spinal form with added isolated involvement of a bulbar-pontine area, manifesting itself in a facial or abducens palsy; (5) a pure bulbar, pontine, or mesencephalic form, which is associated with isolated involvement of one or two cranial nerves as a result of their particularly low threshold to damage (isolated paralyses of deglutition, circulation, and respiration); and (6) a combined bulbar-pontine-mesencephalic form with severe deficits in the region of the medulla, pons, and midbrain, which are manifested by respiratory paralysis and inability to swallow.

The author recommended active immunization of all children over six months of age and adults up to the age of 40, especially pregnant women, by intramuscular or subcutaneous injections of Salk vaccine, and passive immunization with human gamma globulin during epidemics if there is a history of contact. As treatment of clinical poliomyelitis Hertl suggested rest for the first six days or during the febrile period in order to protect the ganglion cells against chromatolysis. The patient should be kept in a darkened room in quiet surroundings and short-acting sedatives should be given. Appropriate positioning should be accomplished with sand-bags, splints, plaster casts, and bandages. Passive and, later, active exercises should be begun about eight days after the subsidence of the fever. Treatment of the edema in all patients with signs of encephalitis and combined bulbar-pontine-mesencephalic involvement was by means of 20 to 25% human albumin, 40% dextrose solution (3 to 5 ml. per kilogram of body weight three times a day), or 1 to 4 ml. of horse chestnut extract with thiamine three times a day and large doses of vitamins C and P intravenously. Treatment of paralysis of the muscles of deglutition was by postural drainage, suction, and prophylaxis against pneumonia (antibiotics by mouth, tube-feeding, or tracheotomy). Treatment of respiratory paralysis was by continuous artificial respiration, if necessary after previous tracheotomy, regardless of whether the respiratory insufficiency was of central or peripheral origin. Circulatory disturbances were successfully treated with a 5 to 10% dextrose solution supplemented by vitamins C and P, with levarterenol, nikethamide, Effortil, and horse chestnut extract with thiamine. In patients with hyperpyrexia, treatment by means of exposure, ice packs, aminopyrine, or phenothiazine derivatives proved of value.

Revaccination Against Smallpox.—W. Ehrengut, of Munich, stated that in view of the dangers of postvaccinal encephalitis associated with first vaccination at a late age it is advisable to examine all candidates for revaccination for the presence of vaccination scars, because these scars are proof of a successful engagement of the body with the vaccinia virus. Often, however, candidates for "revaccination" appear who have no vaccination scars but are yet able to produce valid certificates of vaccination. The author found in 1956 that in a series of 9,511 children 751 had no visible vaccination scars. Of these, 171 had valid vaccination certificates. These 171 candidates for "revaccination" were then vaccinated with the result that 71 developed a primary reaction, 80 gave an immune reaction, 10 gave a vesicular reaction, and 10 gave an accelerated pustular or vaccinoid reaction. Inquiries from parents or guardians elicited the statement that the remaining 580 children with no vaccination scars had not been vaccinated before. In some of these vaccination was indefinitely postponed. Others were vaccinated with the consent of the parents.

The fact that 80 of 171 children with no vaccination scars showed an immune reaction to vaccination, reacting as though they were in fact being revaccinated, was surprising. Apparently the primary vaccination, which had been performed, on an average, nine years before, left an adequate immunity even though it had left no visible scar. The vesicular reaction and the accelerated pustular reaction also indicated in a further 20 children some degree of previous immunization. In the opinion of Ehrengut the absence of the primary scar in candidates for revaccination can be explained by (1) a scarification which had been kept small for cosmetic reasons or from fear of neural complications, (2) the formation of very small vesicles as a result of a delayed reaction, either because the vaccine was of low virulence or because the child already had a high resistance, or (3) individual variations in scar-tissue formation which do not run parallel with the degree of immunity acquired.

From statistics on smallpox in Germany it appears that vaccinated children who have no vaccination scars do have a certain degree of immunity. Ehrengut recommended that candidates for revaccination who show no primary scar but have a valid certificate of vaccination should be revaccinated only after the success of the primary vaccination has been confirmed by the parents.

Hyperketonemic Diabetic Coma in Children.—Krainick and Tittmann (*Arch. Kinderh.* 159:15-28, 1959) stated that the hyperketonemic form of diabetic coma is characterized biochemically by a severe ketosis which is in contrast to a moderate hyperglycemia. A further characteristic is the persistence of the ketosis, which, even after several days' treatment, may give rise to relapses into coma. The ketosis is generally associated with an acidosis, which is recognized clinically by the typical Kussmaul respiration and biochemically by a greater or lesser reduction in the alkaline reserve. Dehydration is less marked than in the hyperglycemic form of diabetic coma. The authors distinguished a spontaneous and an artificial form of hyperketonemic coma. The artificial form was attributable to overdosage of insulin without sufficient intake of sugar. The spontaneous form was probably due to an individual, probably constitutional, peculiarity and was most frequently seen in infants.

Treatment consisted in the timely and adequate administration of sugar with relatively small doses of insulin. Whereas insulin is the first requirement in the treatment of hyperglycemic coma, and to give initially large quantities of sugar to patients with this type of coma may have unfortunate consequences, in the treatment of hyperketonemic coma prompt, large, and continual doses of sugar are necessary. Oral administration of glucose should begin, at the latest, when the blood sugar level reaches 200 mg.%.

The best infusion mixture is an alkaline solution of electrolytes in equal parts with a 20% levulose solution. This is best given by intravenous drip; 5 to 10 units of insulin should be injected into the upper part of the transfusion tube, first at half-hourly intervals, then every hour or two. In general, about 250 ml. per hour should be given for a total of four hours or longer if necessary. The blood sugar level should be estimated every half hour and the ketone level every hour. Juices rich in potassium (lemon, orange, or carrot juice) are sufficient to prevent the hypokalemia which is likely to occur once diuresis has begun. The unique pathogenic character of the hyperketonemic form of diabetic coma is founded on the increased tendency of the child to ketosis. The hyperketonemia of the coma is attributed to central nervous stimulation, which gives rise to a much greater fat mobilization than that usually founded in diabetic coma.

INDIA

Piperazine Salts for Ascariasis.—Vora and Vasi (*J. Indian M. A.* 33:8 [Oct. 16] 1959) stated that some workers have found that the efficacy of piperazine preparations is related directly to the content of the base irrespective of the nature of the salt, as judged by the clearance of ova of Ascaris lumbricoides from direct fecal smears or as judged by stool examination with use of formalin-ether sedimentation method and by ova count. Others found that the cure rate with the piperazine citrate was 77% for ascariasis while with the adipate it was 95%, as judged by the number of patients rendered free of ova.

The authors, therefore, compared the vermifuge action of piperazine citrate, adipate, tartrate, and phosphate. A series of 112 patients received the citrate, 100 the adipate, 130 the tartrate, and 100 the phosphate. The dose for patients above the age of 12 years was 3 Gm. of the base. After the last meal at 7 p. m., the drug was given at 2 a. m. followed by a soapsuds enema at 6 a. m. All the stools passed for four days after therapy were examined for adult worms. Patients who passed no worms during this period were considered to have obtained a negative result. The percentage of positive results was 47.3% with the citrate, 84% with the adipate, 23.1% with the tartrate, and 20% with the phosphate. In the case of each salt the positive response declined with patients' advancing age. Thus, those under 21 years of age showed better results than did those 21 or over.

The worms expelled after administration of the phosphate and tartrate were rigid, straight, and nonmotile, while those expelled after the citrate and adipate had been given were normal in appearance, soft, and motile. The change in the worms may have made it difficult for them to pass through various segments of the intestinal tract. The authors concluded that piprazine citrate was the most effective preparation, the adipate next, with little choice between the tartrate and phosphate.

Misuse of Milk Powder.—The Union Health Ministry requested organizations receiving milk for free distribution under the Indo-United States agreement to take all possible care in the distribution of milk powder so that it is not misused and sold in the market. Complaints have been made from time to time that milk received for distribution to the poor is being sold in the open market. The milk received from UNICEF and the U. S. Technical Cooperative Mission (TCM) comes in powdered form and is generally distributed in liquid form through various child welfare and primary health centers. Several voluntary agencies in the country receive milk from such organizations as the Cooperative for American Remittances to Everywhere (CARE), Catholic Relief Service, National Catholic Welfare Conference, and National Christian Council of India. The Indian Red Cross Society also gets milk powder, which is distributed through its state and district branches, to whom strict instructions have been given regarding its proper use and accounting. The society distributes milk in liquid form in order to minimize possible misuse. The quantity made available to the Indian Red Cross Society is only a small portion of the total milk supplied to this country under the Indo-United States agreement.

Diphtheria.—Parikh and Thanawala (*Indian J. Child Hlth.*, 8:10 [Oct.] 1959), in a study to correlate the clinical features of diphtheria with the different types of Corynebacterium diphtheriae, found that infection with the mitis strain accounted for 80% of the cases in their series of 127 patients. Swabs from different sites from the same patient showed the same type of organism, there being no mixed infections. From swab studies, 17.6% were found to be of the gravis and 2.4% of the intermedius type. In this series 114 patients were under 10 years of age. None had been immunized against diphtheria. Fever, salivation, and vomiting were more common in gravis infection, while pain in the throat, cough, swelling of the neck, hoarseness, and otalgia were more common in mitis infection. The mitis strain was more common in laryngeal diphtheria and the gravis strain in the "bull neck" variety. All patients who had laryngeal diphtheria with respiratory obstruction were under 6 years of age. Diphtheria antitoxin was given to all patients on admission. Procaine penicillin G or broad-spectrum antibiotics also were given until the membrane disappeared. Six patients died and 11 became carriers. Paralytic complications were infrequent in those with the gravis strain and were relatively mild. Paralysis occurred in 25% of those with mitis infection.

UNITED KINGDOM

Boxing.—The abolition of boxing was urged in *Lancet* (Nov. 7) for the second time in five months because the sport can unquestionably produce punch-drunk imbeciles. Recalling that on Oct. 26 a bantam-weight boxer from California died in Mexico from cerebral hemorrhage two days after a world championship bout, the writer pointed out that this death coincided with a discussion at the Medical Society of London on the hazards of boxing. Although professional boxing found no advocates in the discussion, opinion on amateur boxing was not unanimous. Some claimed that it is a wholly admirable character-building activity, free from material risk, and a useful safety-valve for aggressive instincts.

Cross Infection in Hospitals.—Methods to prevent staphylococcic cross infection in surgical wards were described by Gillespie and co-workers (*Lancet* 2:781, 1959). Before preventive measures were taken nearly 40% of open wounds became infected by staphylococci in the wards, although most of these were detected only by bacteriological tests and were of little or no clinical significance. Cross-infection was responsible for 3% of the patients developing other staphylococcic infections such as bronchopneumonia, enterocolitis, furunculosis, parotitis, urinary infection, and wound sepis at operation. One factor in the spread of infection in the operating room was contaminated air drawn in from the wards. Modification of this did not lower the incidence of operating-room infection, although the installation of an up-to-date ventilating plant would probably have done so. Reduction of infection in the wards, however, reduced that in the operating room.

Preventive measures taken over a period of a year reduced the staphylococcic cross infection of wounds from 40 to 4%. Among the measures taken were the nasal disinfection of patients and staff with a water-miscible cream containing neomycin and chorhexidine; treatment of blankets and pillows with formaldehyde vapor, which reduced the bacterial count by 95% without harming the fabrics; the disinfection of crockery, cutlery, shaving equipment, and baths with substances such as chlorhexidine, sodium hypochlorite solution, and alcohol; the spraying of all open and draining wounds with a solution containing neomycin, bacitracin, and polymyxin (Polybactrin); the exclusive use of disposable paper towels; and the use of soap containing hexachlorophene, which was also added to washing water. Dust was kept down by vacuum cleaning throughout the hospital. It could not be ascertained which precautions were chiefly responsible for the fall in staphylococcic infections but no one precaution alone was considered sufficient. An intelligent understanding of the purpose of all these precautions, by those concerned, was of great importance.

Radioactive Contamination of Food.—The Radiobiological Laboratory of the Agricultural Research Council issued a report on its work on the contamination of food and agricultural land by radioactive substances (Strontium-90 in Human Diet in the United Kingdom, Her Majesty's Stationery Office, 1959). Strontium-90 (Sr^{90}) which has a comparatively long life, is deposited with calcium in newly formed bone, where it irradiates the marrow. Its concentration in the body is determined by its ratio to calcium in the diet, as it follows the same metabolic pathways. Radiation hazards from Sr^{90} are estimated as micromicrocuries per gram of calcium ($\mu\mu$ c/Gm. Ca). The maximum allowable concentration of Sr^{90} in bone has been fixed at 100 $\mu\mu$ c/Gm. Ca. Although this is unlikely to be reached, Sr^{90} accumulates, and any rise in concentration in human bone must be seriously considered.

Of the food consumed, milk accounts for 54% of the Sr^{90}, flour for 12%, cheese for 11%, green vegetables for 10%, meat for 4%, drinking water for 4%, fruit for 3%, eggs for 0.6%, and fish for 0.2%. White flour contains added calcium, but wholewheat flour does not. As in addition the Sr^{90} content of bran is seven times that of white flour, the daily intake of Sr^{90} would be increased from six to nine $\mu\mu$ c/Gm. Ca if white flour in the diet were to be replaced by wholewheat flour. In some localities the amount of Sr^{90} in the diet is six times the average. This is due to atomic fall-out being localized in some areas.

At the British Association Meeting at York last September, it was asserted that on a high carbohydrate diet a quarter as much radium and thorium may be ingested as is permanently fixed in the bones. The amounts of these radioactive substances in fruit, vegetables, and animal and fish products are low, but they are high in cereals, white flour, and nuts. The highest alpha-particle activity, which is a measure of the concentration of radium and thorium, was found in Brazil nuts, 120 Gm. of which contained as much as the whole body. Apparently a high intake of radium and thorium in the diet does not lead to their excessive storage, unlike Sr^{90}, the level of which is slowly rising in the body.

Hypothermic Coma from Chlorpromazine.—Mitchell, Surridge, and Willisone (*Lancet* 2:932, 1959) reported the case of a woman on whom a partial thyroidectomy was performed in 1944. She was well until 1958 when she complained of feeling cold and developed a myxedematous psychosis, for which she was admitted to a mental hospital. As she was maniacal and violent and screamed persistently, she was given 100 mg. of chlorpromazine intramuscularly. The next day she went into a coma and could not be roused. She was fat and pale and had a cold dry skin and a rectal temperature of 92 F (33.3 C). No peripheral pulses could be felt and the blood pressure was unrecordable although heart sounds could be heard. The diagnosis was myxedematous coma, precipitated by chlorpromazine.

The patient was immersed up to the neck in water at 208 F (98 C) and given 40 mcg. of tri-iodothyronine intravenously. Four hours later her rectal temperature was 100 F (37.8 C). She was then removed from the bath and put in a warmed bed. A second injection of 40 mcg. of tri-iodothyronine was given. The blood pressure rose steadily. Further injections of tri-iodothyronine as well as hydrocortisone were given. The patient made a complete mental and physical recovery. This case is unusual, as hypothermic myxedema coma is generally fatal. Survival was attributed to the intravenous use of tri-iodothyronine which acted within a few hours. The hydrocortisone corrected transient adrenal insufficiency, which was shown to be present.

Diagnosis of Systolic Murmurs.—Accurate interpretation of systolic murmurs is always important but sometimes difficult, and may require phonocardiography or the use of certain well-established maneuvers, such as exercise or the Valsalva test. Vogelpoel and co-workers used the inhalation of amyl nitrite to distinguish the various types of systolic murmur (*Lancet* 2:810, 1959). When this substance is inhaled it causes a sudden vasodilatation resulting in a rapid fall in systemic blood pressure, tachycardia, and increased cardiac output. This is followed by a greatly increased venous return to the right heart. The effect is maximal at the end of an inhalation lasting 30 seconds and persists for 20 to 30 seconds after the patient ceases to inhale the drug. Left-sided regurgitant systolic murmurs become softer and shorter during and for about 20 minutes after the inhalation, the mechanism being dependent on the fall in systemic blood pressure, which reduces regurgitant flow. Such murmurs are caused by mitral incompetence, ventricular septal defect, patent ductus arteriosus with a left-to-right shunt, and systemic arteriovenous fistula.

Right-sided regurgitant murmurs, due to tricuspid incompetence, become louder and longer after the patient inhales amyl nitrite, owing to the increased venous return to the right heart with increased regurgitant flow. Left and right-sided ejection murmurs, with the important exception of those in Fallot's tetralogy, were found to increase in loudness because of increased forward flow. The intensification is greater and more sustained when the murmur is due to stenosis than when it is not. The chief value of the test is in the differential diagnosis of ventricular septal defects from pulmonary stenosis; pulmonary stenosis from mild or acyanotic Fallot's tetralogy; atypical patent ductus from other pulmonary systolic murmurs; aortic stenosis from mitral incompetence; and mitral incompetence from tricuspid incompetence. The test is also said to be of value in assessing whether or not a mitral or tricuspid systolic murmur is due to organic valvular disease. The test is simple and harmless.

Electronic Respirator.—An electronic respirator, which in time may replace the "iron lung," has been built by Mr. Derek Winks. It is called the Barnet ventilator. It was first foreshadowed by Drs. Ronald Welch and James Rochford, both of Barnet General Hospital. Unlike the Drinker respirator, which is heavy and cumbersome and restricts the patient, the ventilator weighs only 56 lb. and is completely portable. Patients using it would have freedom limited only by the length of its two tubes. Although the machine has not been used on patients with poliomyelitis, it might prove suitable for such use. The machine has built-in batteries from which its transistorized circuit will run for up to 20 hours without recharging. Thus the patients with poliomyelitis could be moved from one hospital to another, or by air between continents, without difficulty. The ventilator can be used to help a patient's breathing when it has been weakened from any cause. It can also be used in operating rooms for the administration of anesthetics. In the Barnet group of hospitals it has been used for patients with chronic bronchitis and asthma and those who have had a thoracic operation.

Psychiatry for Clergymen.—Two psychiatrists told a conference of clergymen and voluntary social workers in London that courses in psychiatry should be included in the training of all ministers of religion. The conference was organized by the All-Denominational Central Churches Group to discuss the part churches could play in the problem of mental health. Dr. T. P. Rees said that the best way of dealing with the mentally sick was not to build more and bigger modern hospitals but to find ways of treating them within the community. In 1930 about 20,000 hospital beds in Britain were occupied by mentally sick people. By 1958 the number had grown to more than 100,000. A shortage of nurses is still a problem for most mental hospitals. Dr. D. V. Martin said that while clergymen could not deal with major mental illnesses their potential ability to prevent mental breakdowns was great. They could help to find a home for the patient who had spent several years in a mental hospital and was to be discharged as recovered. Having no relatives or friends to turn to, he or she represents a lost soul.

Primary Hyperoxaluria.—Primary hyperoxaluria is characterized by a continuous high urinary oxalate excretion (100 to 400 mg. daily), which causes extensive urinary stone formation and nephrocalcinosis. The patient usually dies in childhood or early adult life from renal failure or the complications of hypertension. Scowen and co-workers, using radioactive labeled glycine (C^{13}), studied the origin of hyperoxaluria (*Lancet* 2:808, 1959). A dose of 2.56 mg. of radioglycine per kilogram of body weight was given to four patients with primary hyperoxaluria. The oxalate was isolated from successive six-hour specimens of urine and the C^{13} content was measured. The oxalate isolated from the first urine specimen contained C^{13}. The amount of the latter increased for 18 to 24 hours after the labeled glycine was given and then remained fairly constant. It was calculated that the carbon skeleton of 33 to 50% of the urinary oxalate was derived from the glycine adminstered, probably via glyoxalate. The data obtained were compatible with the view that primary hyperoxaluria is an inborn error of metabolism involving failure to break down glyoxalate normally.

A normal subject was given labeled radioglycine, and the urine examined in the same way as for the oxaluric patients. Estimation of the urinary excretion of labeled oxalate showed that about 40% of it was derived from glycine. This figure is comparable with those obtained from the patients with hyperoxaluria.

Malignant Hypertension.—Dr. M. Harington and co-workers (*Brit. M. J.*, Nov. 14, 1959) used ganglion-blocking drugs in the treatment of a series of 82 patients who had malignant hypertension. The expectation of life of the treated patients was increased by a factor of six to eight compared with that of a control series previously reported from the same hospital. Prolonged survival was particularly seen in those patients whose renal function was normal or only slightly impaired at the start of treatment. Death was most frequently due to uremia. Heart failure as a cause of death was greatly diminished in the treated group. The benefits of treatment were most pronounced in retinitis and myocarditis. Improvement in the electrocardiogram was seen in 33%, but reduction in cardiac size occurred less frequently.

Renal function tended to remain stationary or to improve slightly in patients with an initial blood urea level below 80 mg. per 100 ml. If renal impairment was more severe than this, progressive deterioration was the rule. Patients with neurological complications did not derive much benefit from treatment. Accompanying atherosclerosis was a limiting factor in the success of treatment, particularly in older patients. A survey of the histological lesions in the kidneys showed that after treatment with hypotensive drugs the main changes were a conversion of cellular intimal hyperplasia in the interlobular arteries to fibrous intimal thickening and a "healing" of fibrinoid degeneration to hyaline and fibrous tissue. Some correlation was likely between the degree of narrowing of the interlobular arteries at the start of treatment and the prognosis.

CORRESPONDENCE

SPONTANEOUS DISAPPEARANCE OF GALLSTONES

To the Editor:—In the article "Spontaneous Disappearance of Gallstones" in The Journal, Oct. 24, page 1098, the case history is most interesting, but the fact remains that only one recheck of the cholecystogram (Oct. 16, 1958) was made. It is possible to see in figure *D* the same stones as are seen in *A* and *B*. Everything I have said so far is based on the fact that I can see the stones in *D*, as can my colleagues, but whether the stones are visualized or not in *C* and *D*, I do not believe that this is worthy of report until this patient has had repeated cholecystograms, an exploratory operation to rule out the stones, or postmortem examination to show their absence.

William B. Hobbins, M.D.
1 S. Pinckney St.
Madison, Wis.

This item was referred to the authors of the original article, and the following reply was received.

To the Editor:—Dr. Hobbins objects to the soundness of a report of pathological change based on extensive, clear-cut roentgenologic evidence. He apparently believes that the only way to prove such change is by postmortem examination, surgical excision, or repeated x-ray studies. I differ with him on this point. Unequivocal roentgenographic demonstration (or nondemonstration) of pathological material is fully as acceptable as a surgical specimen or postmortem proof. Repeated studies may be necessary at times, but in this instance a further recheck would have been superfluous, since the recheck was so exhaustive and conclusive at the time it was accomplished.

Dr. Hobbins states that "only one recheck of the cholecystogram was made." The recheck did not consist of one cholecystogram but of at least 20 exposures made with the patient in varying degrees of rotation in prone, supine, and upright positions before and after the administration of a fatty meal. In addition, compression spot film studies of the gallbladder were made with the patient recumbent and upright. In none of the many films was there any suggestion of gallstones. The rarity of the situation demanded this exhaustive study. Later, in view of Dr. Hobbins' letter, we made another exhaustive study of the gallbladder about 12 hours after oral ingestion of bunamiodyl sodium, consisting of numerous films in both prone and upright positions before and after a fatty meal. There was no sign of any abnormality in the gallbladder, which showed normal opacification and no evidence of stones.

Reproductions of roentgenograms rarely do justice to the original demonstration of findings. Therefore, I suggest that Doctor Hobbins view the films directly. I will be happy to send all of the roentgenograms to him, so that he and his colleagues may be convinced that the gallstones actually disappeared.

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CRITICISM OF CRITICISM

To the Editor:—A review of "Current Problems in Allergy and Immunology" appeared in The Journal, Oct. 31, page 1270. Traditionally, there is no appeal from the pronouncements of those who review books, but the reviewer of this book has taken a position so extreme that he is open to serious criticism. Excepting a handful of papers in the volume, which are devoted to basic research, he characterizes the work as "poor," "mediocre," and "faddish."

In assessing the value of the work of a full 100 contributors, a reviewer might be expected to choose examples of material with which he could not agree, but there is something ridiculous about any critic, no matter how eminent, who condemns the work of so widely representative a group as being "likely to mislead the uninformed reader" and "recommended only to those who already possess a good, discriminative acquaintance with the field." In one stroke he calls into question not only the abilities of the writers but the discriminatory powers of readers.

The authors of the work in question not only have prepared a complete and balanced digest of current thinking in this field but have done much to bring together allergists and immunologists of the free world. It is regrettable that this work has been subjected to such harsh and arbitrary judgments.

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MEDICAL FILM REVIEWS

Suprapubic Transvesical Prostatectomy: 16 mm., color, sound, showing time 20 minutes. Prepared in 1959 by Leonard V. Smiley, M.D., New York. Produced by Sturgis Grant Productions, New York. Procurable on loan from Leonard V. Smiley, M.D., 960 Grand Concourse, Bronx, N. Y.

The purpose of this film is to demonstrate the author's modification of the classic one-stage suprapubic transvesical enucleation of the prostate, which permits the patient to void voluntarily from the second postoperative day. The safety feature of temporary suprapubic tube drainage is retained. The technique is essentially that of the classic transvesical enucleation with excision under vision of remaining nodes and tabs of tissue. A wedge resection of the posterior bladder neck is done. Hemostasis is obtained by figure of eight sutures placed at 5 and 7 o'clock through the prostatic capsule, with use of a boomerang needle. A Foley catheter is left in the urethra. The bladder is closed, after the method of Hrynschak, with a purse-string suture and a suprapubic tube brought out of the bladder through a stab wound in the abdominal wall. The Foley catheter is removed on the second day and the patient voids at will. The suprapubic tube is removed on the sixth day. The author does not discuss complications in detail. The photography is good and is supplemented with drawings by Dr. Frank Netter and Stephen R. Peck. The film is recommended for urologists, residents, and interns.

Undescended Testis: Surgical Anatomy of Spermatic Vessels, Spermatic Surgical Triangles and Lateral Spermatic Ligament: 16 mm., color, sound, showing time 23 minutes. Prepared in 1959 by Robert J. Prentiss, M.D., C. J. Weickgenant, M.D., J. J. Moses, M.D., and D. B. Frazier, M.D., San Diego. Procurable on loan from Robert J. Prentiss, M.D., 3415 Sixth Ave., San Diego 3.

This film combines anatomic charts, x-rays, and animated schema with dissection of the cadaver to demonstrate the steps in the developing of adequate cord length. The second part of the film demonstrates the problems of an operation performed on a living patient. Adequate length of the cord with proper placement of the testicle deep in the scrotum is obtained by dissection of the spermatic vessels, cutting of the deep epigastric vessels, and incision of the floor of the inguinal canal. The film presupposes a fundamental surgical knowledge of the normal inguinal anatomy, which is not presented in detail. Preoperative and postoperative views of the patient would have added to the presentation, and it requires great concentration to follow all of the steps presented in the drawings and x-rays. This would have been much easier for the viewer if the various details had been pointed out. It is fundamentally a good teaching film and is recommended for urologists, general surgeons, residents, and interns.

Cerebral Vascular Disease: The Challenge of Management: 16 mm., black and white, sound, showing time 39 minutes. Produced in 1959 by George C. Stoney Associates for the American Heart Association with the assistance of a grant from E. R. Squibb & Sons. Procurable on rental and purchase from the American Heart Association Film Library, 267 W. 25th St., New York City 1.

The film is designed to acquaint general practitioners and nurses with the management of patients suffering from strokes. A tentative survey of the more promising therapeutic measures now being tested by clinical investigators, which require the collaboration of general practitioners with surgeons and internists, is presented in the first eight minutes. The remainder of the film describes the management of an elderly man with moderate hemiplegia on the left. The patient is treated in a small hospital without physical therapy facilities. Prevention of deformity during the acute phase is stressed along with measures to preserve life. The family is instructed in rehabilitation procedures while the patient is in the hospital, and home care is supervised by the physician and the visiting nurse. Simple home exercises and training to help the patient walk and take care of himself are well described. Emotional and social problems of the patient and his family are given proper emphasis, and the value of continued guidance by an interested and sympathetic doctor is stressed. The rehabilitation section of this film is excellent both technically and educationally. The photography and the production techniques in the film are very good. Narration is clear and authentic. Suitable audiences would include medical students, nurses, and families of hemiplegic patients; the film is highly recommended for general practitioners.

Some Techniques of Tissue Section Preparation in the Pathology Laboratory: 16 mm., color, sound, showing time 29 minutes. Sponsored by and procurable on purchase and preview loan from National Committee for Careers in Medical Technology, 1785 Massachusetts Avenue, N. W., Washington 6, D. C. Produced in 1959 by Jack Churchill, Boston, under the supervision of Maurice N. Richter, M.D., New York City.

This motion picture, which deals with histologic technique, is a masterpiece in didactic presentation of a subject which will be of great interest to medical technologists, to students of medical technology in the many schools of medical technology in the States, and to pathologists in general. The newest techniques are shown clearly and correctly. It is well organized and produced with strong emphasis on sources of error in technique, which lead to endless troubles if not heeded. The cinephotomicrographic footage demonstrating proper compared with improper tissue techniques with the split-screen method is of a photographic quality that is impressive. Color and definition are excellent. Narration is clear and concise. This film is recommended without reservation to medical technologists and to anyone engaged in tissue preparation or reading.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Palpation of the Heart in the Diagnosis of Ventricular Hypertrophy: Apical Murmur of the Right Ventricle as a Sign of Pure Pulmonary Stenosis. A. S. Cascos, P. de Rábago-González and M. Sokolowski. Rev. clin. españ. 74:8-14 (July 15) 1959 (In Spanish) [Madrid].

Twenty cardiac patients were examined by palpation, and the data thus obtained were compared with roentgenologic, electrocardiographic, and catheterization data regarding their diagnostic value. The palpation technique presented by the authors consists of 2 phases: (1) an inspection of the epigastric, pulmonary, and sternoclavicular areas for detection of any anatomic abnormality; (2) a methodic palpation of the same areas for observation of heart murmurs, tonus, and fluttering. The 20 patients studied also underwent a complete roentgenologic examination, especially of the apical characteristics, complete electrocardiographic study, and catheterization with study of the systolic pressure in the right ventricle. Congenital cardiopathy was diagnosed in 15 patients, and mitral stenosis in 5.

The palpation of the cardiac area was of especial value in establishing the diagnosis in 2 groups of patients—those with pulmonary stenosis without interventricular communication, and those with a single ventricle. In the first group the massive hypertrophy of the right ventricle caused a strong, full, and long apical murmur which pushed the palpating finger upward and outward instead of inward and downward. This is caused by the fact that the hypertrophied right ventricle eventually becomes the whole heart apex. In the patients with a single ventricle, the palpation revealed an apical murmur typical of left ventricle hypertrophy, but gave no signs of a right ventricle hypertrophy in either the epigastric or the sternal area on the left. As the catheter entered the right ventricle, there was a strong hypertension, in contradiction to the lack of signs of right ventricle hypertrophy during palpation. This contradiction seems to be due to the absence of the interventricular septum. The authors believe that cardiac palpation may be as valuable as the roentgenologic and electrocardiographic examination for the diagnosis of ventricular hypertrophy and that it is a useful method in the diagnosis of a complicated hypertrophy and a hypertrophy of the trabecular area, which give no electric signs.

Iproniazid in the Treatment of Coronary Insufficiency. L. Abecasis and F. Trocolo. Bol. clín. hosp. civis Lisboa 23:29-45 (Jan.) 1959 (In Portuguese) [Lisbon].

Twenty-four patients (12 men and 12 women), with a diagnosis of coronary insufficiency established by clinical examination and electrocardiography, were treated with iproniazid during periods which varied between 15 days and 4 months. They were treated as outpatients and examined every other day at the beginning of the therapy, then weekly. Their blood pressure was checked every week, and an electrocardiogram was taken every other week. The initial dose of iproniazid was 100 mg. daily (50 mg. every 12 hours); this was reduced to 50 mg. daily after some improvement had been obtained or when there were serious untoward reactions to the drug. All previous medication was suspended during the 15 days preceding the start of the iproniazid treatment, except for the patients with diabetes and those who were taking Tromexan. Patients on a low-salt and/or a diabetic diet were kept on the same diet.

Clinical response to the therapy appeared between the 7th and the 45th day of treatment. Angina pectoris disappeared entirely in 16 patients, improved slightly in 7, and remained unchanged in 1. Favorable electrocardiographic changes were observed in 8 patients whose electrocardiograms had shown signs of coronary ischemia. In 7 of these there was total remission of pain, whereas in 1 there was only slight improvement. In 7 other patients with electrocardiographic signs of ischemia, there was no electrocardiographic improvement, although in 4 of them the pain had disappeared and in 3 it was much better. In 6 patients with signs of previous infarction, there was no electrocardiographic change, although 3 were completely relieved from pain and 2 were slightly improved. In 3 patients with aortic insufficiency there was no electrocardiographic change, although 2 of them experienced

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The place of publication of the periodical appears in brackets preceding each abstract.

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total clinical relief and the third had partial relief.

The numerous unfavorable reactions were gastrointestinal in 8 patients, urogenital in 5, and neuropsychic in 11; 8 patients had edema of the lower extremities, and 6 had hypotension. In 14 patients the dose had to be reduced to 50 mg. daily because of side-effects. In 6 of these the pain recurred. In all the patients who for some reason interrupted the treatment and experienced a recurrence of pain, the therapy was repeated, and the same results were obtained as after the first treatment. The authors believe that iproniazid has a twofold activity —an anabolic effect on the myocardial metabolism and a blocking effect on the autonomous nervous system. The remission of pain without a concomitant change in the electrocardiogram suggests that a direct action of iproniazid on the coronary vessels is doubtful. In the patients who obtained both pain relief and favorable electrocardiographic changes, the effect of iproniazid on the autonomous nervous system had probably been more pronounced, which indirectly caused a better coronary vasodilatation.

The Gastroduodenal Ulcer in High Altitudes (Peruvian Andes). G. Garrido-Klinge and L. Peña. Gastroenterology 37:390-400 (Oct.) 1959 [Baltimore].

Of 3,845 patients admitted to the Hospital Obrero in La Oroya, Peru, between June, 1953, and April, 1955, 79 had gastroduodenal ulcer. This gives an incidence of 1.85% among the hospitalized population and a 0.4% general incidence of gastroduodenal ulcer. The hospital is situated at an altitude of 12,240 ft. (4,100 meters) and takes care of insured laborers (chiefly miners) living in the Peruvian Andes at altitudes ranging from 10,000 to 16,000 ft. (3,300 to 5,300 meters). Of the 79 patients, the authors report on 71 in whom the diagnosis of gastrointestinal ulcer was confirmed by x-ray findings or on surgical intervention. Of the 71 patients, between the ages of 19 and 69 years, 69 were men and 2 were women. Thirty-four (48%) of them were between the ages of 21 and 30 years. The predominance of men is explained by the fact that most of those insured were men; the only 2 women were relatives of hospital employees, but among 106 insured women there was not a single case of ulcer.

All the patients except 2 were born and lived in the high Peruvian Andes. The most notable symptom was digestive hemorrhage, which reached the high proportion of 66%. There was a high incidence of focal infections (tonsils or teeth or both), amounting to 52%. Generally the oral hygiene was very bad, and masticatory insufficiency was high. Of the 71 patients, 62 had gastric ulcer, 6 had gastric and duodenal ulcer, and 3 had duodenal ulcer; the ratio of gastric to duodenal ulcer thus was 20.6 to 1. Forty-three patients (61%) were operated on; 42 underwent subtotal gastrectomy and 1 had a suture of free perforation. The indications for surgical intervention consisted of hemorrhage in 32 patients (45%) and of geographical factors in 10 (14%).

These data reveal most unusual facts, i. e., the great proportion of gastric ulcers as compared with duodenal ulcers, the high incidence of hemorrhage, and the early age at which the gastric ulcer appears. These facts lead to the belief that in the Andean native there may be combined a series of special conditions which make the gastric mucosa more vulnerable to ulceration and likewise more prone to bleed. In high altitudes the vascular and hematic factors, as well as chronic stress (abrupt climatic changes from intense cold to intense heat, chronic anoxia, deficient nutrition, and emotional factors), play a most important role in the pathogenesis of gastric ulcer.

The Changing Pattern of Life-Threatening Microbial Disease. D. E. Rogers. New England J. Med. 261:677-683 (Oct. 1) 1959 [Boston].

In order to determine the incidence and nature of infections contributing to deaths on the medical service of the New York Hospital, the clinical records, laboratory data, and autopsy protocols of 200 consecutive medical-service patients subjected to postmortem examination between 1938 and 1940 and an equal number of those dying in 1957 and 1958 were analyzed in detail. Bacteriological data obtained from clinical or postmortem specimens were correlated with clinical, laboratory, and histological information in deciding whether infection was or was not present. The setting in which infection arose, the clinical course of the illness, and the nature of the death were evaluated in weighing the importance of infection. In the preantimicrobial period, infections caused the death of 57 patients (28.5%) out of the 200 subjected to autopsy. An additional 51 patients (25.5%) had infections of less significance. During 1957-1958, 28 (14%) of the 200 patients died as a direct result of microbial infections. Significant but less critical infections were present in an additional 30 patients. Thus, although a reduction in the total number of fatal infections occurred, microbial disease continued to play an impressive part in deaths occurring within a medical unit.

Striking differences were noted between the 2 periods under study in the microbial parasites that produced fatal disease, the place where infection was acquired, and the presence of unassociated disease antedating infection. In the preantimicrobial period the majority of fatal infections were produced by pneumococci, streptococci, tubercle bacilli, and staphylococci. These infections commonly arose in otherwise healthy persons in the outside community and were the direct cause of hospitalization. In contrast, fatal infections observed in 1957-1958 were commonly caused by gram-negative bacilli, staphylococci, viruses, and fungi, and commonly arose within the hospital in patients already compromised by other serious diseases. Contrary to general belief, fatal staphylococcic infections were not commoner in the postantimicrobial period. Antibacterial drugs appeared to select the microbial agents that could produce disease, but did not prevent infection from arising in patients with abnormal resistance to infection already hospitalized with other processes.

The Clinical Pictures of Pulmonary Tuberculosis in Diabetic Patients. N. Marinelli. Minerva med. 50: 2941-2944 (Sept. 19) 1959 (In Italian) [Turin, Italy].

A study of the clinical picture of pulmonary tuberculosis in 50 diabetic patients is reported. Three of the patients were under 30 years of age and suffered from diabetes of the juvenile type; the other patients were already in the diabetogenic age when they developed tuberculosis. Diabetes was treated in some patients with 10 to 70 units of insulin per day and in the others with sulfonylurea derivatives given in various doses. Forty-six patients presented lesions of the exudative and destructive type: 24 patients presented nodular lesions, mostly of the infiltrative and bronchopneumonic form; 4 presented chronic miliary infiltration with secondary tuberculous orientation; 2 presented miliary tuberculous infiltration; and 16 presented a picture of chronic tuberculosis. The productive type prevailed in the remaining 4 patients of the series, and they were classified as having lesions with primitive chronic basis.

Tuberculosis was treated in all 50 patients with streptomycin or with a combined antibiotic therapy. The effect of the treatment in some instances was not as good and as lasting as it was in nondiabetic patients. Relapses were frequent. Poor results were obtained in 7 patients treated by pneumothorax; only one patient with juvenile diabetes derived benefit from this type of treatment. Nine (18%) of the 50 patients died—7 of tuberculosis, 1 of circulatory insufficiency, and 1 of diabetic coma. The author believes that an involvement of all phases of metabolism is present in the course of diabetes and that the peculiar reactions of the body to Mycobacterium tuberculosis is due to disturbance of the water-salt metabolism.

Treatment of Tapeworm Infection in Man. W. H. Jopling and A. W. Woodruff. Brit. M. J. 2:542-544 (Sept. 26) 1959 [London].

The authors report on 240 patients, 238 of whom were infected with Taenia saginata, one with T. solium, and one with Diphyllobothrium latum. There were 233 adults and 7 children. No statistically significant difference in results was observed between 5 different methods of treatment, including administration of male fern orally or by duodenal tube, administration of quinacrine (mepacrine) hydrochloride by the same routes, and combined oral administration of quinacrine and male fern. Of the 240 patients, 189 (78.7%) were cured by a single course of treatment; 144 (76%) of these passed the head of the tapeworm, and in 45 (24%) it was possible to presume cure as no segments appeared in the stools during the follow-up period. When treatment failed, segments reappeared, on average, 10 weeks later. Factors which may give rise to poor results when these methods of treatment are employed include inadequate fasting before the institution of treatment, administration of male fern in capsules instead of in a draft, and, when doses of anthelmintics of small volume are administered through a duodenal tube, failure to take into account the amount required to fill the tube before any is delivered from its distal extremity.

Unfavorable false impressions of the efficacy of a method of treatment for tapeworms may be obtained unless patients are followed for at least 4 months in cases in which the head of the worm is not recovered after treatment. Failure of treatment due to vomiting was observed more often among patients treated with quinacrine than among those treated with male fern. As vomiting in patients with T. solium infestation may give rise to cysticercosis, treatment with quinacrine in such patients is best avoided.

Infectious Hepatitis: Detection of Virus During the Incubation Period and in Clinically Inapparent Infection. S. Krugman, R. Ward, J. P. Giles and others. New England J. Med. 261:729-734 (Oct. 8) 1959 [Boston].

These studies were carried out at Willowbrook State School, Staten Island, New York. Since 1953, 500 cases of infectious hepatitis with jaundice have been observed in this institution for mentally defective children. The endemic situation, attempts to control it, and the justification for artificially inducing infectious hepatitis were described previously. The decision to continue the artificial induction of hepatitis with the Willowbrook strain of the virus was made after the following factors had been reconsidered: It was inevitable that most of the newly admitted susceptible mentally retarded children would acquire the infection in the institution at large; infectious hepatitis was especially mild at Willowbrook; facilities were available to provide optimum medical care in an isolation unit; and observations on more than 50 patients revealed that the average experimental disease was even milder than the natural infection.

Only newly admitted patients, whose parents gave consent, were accepted for the study. The subjects ranged between 3 and 9 years of age. On entry they were brought directly to the isolation unit and had no contact with other patients in the institution. The nurses and attendants had minimal contact with other patients and personnel. One physician made serial clinical observations. Since the administration of the Willowbrook strain of the virus was usually followed by hepatitis after 35 to 50 days, and since hepatitis occurring after 60 days was shown to be the result of contact with patients who acquired infection after the shorter incubation periods, the diagnosis of primary hepatitis was limited to cases with incubation periods ranging between 35 and 60 days. The development of clinical jaundice, associated with an abnormal serum bilirubin level (higher than 1 mg. per 100 cc.) and an abnormal serum glutamic oxalacetic transaminase (SGO-T) value, was required for a diagnosis of hepatitis with jaundice. The diagnosis of hepatitis without jaundice was reserved for cases in which the serum bilirubin value was less than 1 mg. per 100 cc. and a crescendo-like rise of SGO-T activity was associated with one or more of the following features: fever, vomiting, hepatomegaly, elevated thymol turbidity or positive cephalin flocculation. Observations on more than 30 jaundiced patients indicated that the serum bilirubin value generally became abnormal on the day of maximum SGO-T activity. Accordingly, in hepatitis without jaundice, the day of maximum SGO-T activity was arbitrarily designated as the end of the incubation period.

Virus was detected in stools and blood during the incubation period and early in the course of the disease. Stools collected at the following intervals were shown to be infective: on the 25th day of the incubation period, or 2 or 3 weeks before onset of jaundice; and 1 to 8 days after the onset of jaundice. Viremia was detected on the third day of jaundice, 3 to 7 days before jaundice, and on the 25th day of the incubation period, or 2 or 3 weeks before the onset of jaundice. Viremia was present in a case of inapparent infectious hepatitis in which an abnormal SGO-T activity was the only manifestation of infection.

Serum Glutamic-Oxaloacetic Transaminase Activity as an Index of Centrilobular Liver Cell Necrosis in Cardiac and Circulatory Failure. N. U. Bang, K. Iversen, T. Jagt and G. Tobiassen. Acta med. scandinav. 164:385-393 (no. 5) (In English) [Stockholm].

This study deals with the possible role of liver damage in the increase of serum glutamic oxalacetic transaminase (SGO-T) activity in myocardial infarction. The SGO-T test was given once or twice daily from 2 days to 1 month before death in 31 patients; 13 of these had acute myocardial infarction, 10 had cardiac insufficiency, and 8 were without cardiac disease. SGO-T values measured during hospitalization were compared with the post-mortem histological findings of the liver. Marked damage to the liver was demonstrated by histological examination in 17 out of 23 patients with cardiac disease. All 7 patients with acute coronary occlusion and unexpectedly high SGO-T values showed the histological picture of severe centrilobular liver cell necrosis. A rough correlation between the degree of centrilobular liver cell necrosis and SGO-T values was observed in all instances. Microscopic examination of autopsy material from the liver of 2 patients revealed evidence of centrilobular liver cell necrosis in the process of healing and resembling incipient cardiac cirrhosis. High SGO-T values were established in these 2 patients several weeks before death. This incidence suggests that centrilobular liver cell necrosis might exacerbate the development of cardiac cirrhosis. The conclusion of this study is that an elevated SGO-T level in patients with acute heart failure may be occasionally caused by circulatory damage to the liver and that it does not necessarily demonstrate the presence of myocardial infarction.

Chemotherapy for the Tuberculin Converter: Results of a Survey of Attitudes Among 424 Tuberculosis Hospitals in the United States. E. V. Bridge and F. J. Ahlfs. Dis. Chest 36:369-372 (Oct.) 1959 [Chicago].

A question concerning the medical attitude in relation to chemoprophylaxis for tuberculin converters was included in a questionnaire mailed to 519 tuberculosis hospitals throughout the United States. The question was: "What is your policy regarding chemotherapy for persons (employees, contacts, etc.) whose tuberculin reactions change from negative to positive within a year and who show no evidence of active tuberculosis by x-ray or other examination?" The other questions in this inquiry were related to policies and practices governing chemotherapy after patients are discharged from the hospital.

Replies were received from 424 hospitals (81.7%). Two hundred seventeen respondents (51.2%) stated that they gave no chemoprophylaxis to tuberculin converters unless a tuberculous lesion developed; 99 (23%) offered treatment to selected patients only; 47 (11%) offered treatment to all tuberculin converters; and the remaining respondents gave undecided or qualified answers, or no answer at all, to this specific question. The distribution of replies on a United States map indicated that the attitude toward treatment of tuberculin converters is more conservative in hospitals located in the eastern and southern regions of the country than in those located in the western and north-central regions. Some respondents for one group of hospitals said that, although they favored the treatment of tuberculin converters without any development of actual lesions, their answer had to be given in accordance with the established policy of the hospitals. The authors anticipate that results of controlled studies on the treatment of large numbers of tuberculin converters will influence the more conservative attitude toward chemoprophylaxis for these persons.

"Stiff-Man" Syndrome. R. E. Whalen, J. J. Combs Jr. and W. P. Deiss Jr. Am. J. Med. 27:678-681 (Oct.) 1959 [New York].

The authors report on a 28-year-old man who was admitted to the Veterans Administration Hospital in Durham, N. C., with a chief complaint of progressive stiffness of the neck for one and a half years. Although the rigidity of the patient's neck muscles fluctuated from day to day, he never had severe spasms. The voluntary cervical muscle groups were noted to be stony hard, nontender, and immobile. The rigidity increased over the next 3 years, and the patient sat with his head hunched forward and face turned upward, forced by the immobile rock-like trunk muscles to pivot his entire body in gazing laterally. His arms were held in a permanent position of partial flexion and abduction. There was minimal involvement of the leg muscles. Neurological examination was normal except for the muscle changes. General anesthesia with intravenously administered succinylcholine chloride failed to produce relaxation of the involved muscles. The patient received no benefit from a 16-day course of phenylbutazone (total dose of 6,000 mg.), intravenous administration of mephenesin, and irradiation to the neck (600 r). Muscle biopsy was consistent with atrophy and fibrosis. Laboratory studies revealed leukopenia (hitherto undescribed) and glycosuria, previously reported by other workers. With the present knowledge, it is impossible to classify this rare disorder, although there is some evidence to suggest that it may be due to a metabolic defect.

Observations on Ceruloplasmin in Wilson's Disease. A. Sass-Kortsak, M. Cherniak, D. W. Geiger, and R. J. Slater. J. Clin. Invest. 38:1672-1682 (Oct., part 1) 1959 [New Haven, Conn.].

The most consistent biochemical abnormality in hepatolenticular degeneration (Wilson's disease) is the deficiency of the copper-containing alpha-2 globulin, ceruloplasmin. It was suggested that a defect in the production of this protein may be the basic metabolic abnormality. This paper describes 2 brothers who had hepatolenticular degeneration and normal serum concentration of ceruloplasmin. These 2 patients were investigated in detail, including studies with radiocopper (Cu^{64}), in order to substantiate their diagnosis and also in the hope that the results might contribute to the knowledge of the basic mechanism of hepatolenticular degeneration.

Practically all the typical features of hepatolenticular degeneration were present in the 2 brothers, but the blood levels of ceruloplasmin were normal. One of them, in spite of the presence of normal blood levels of ceruloplasmin, showed a marked delay in the rate of incorporation of Cu^{64} into ceruloplasmin. The authors feel that the normal blood levels of ceruloplasmin in 2 otherwise typical cases of hepatolenticular degeneration suggest that a defect in the production of ceruloplasmin may not be the basic metabolic abnormality in this condition, or at the least not in all cases. Nevertheless, the observation of a marked delay in the rate of incorporation of Cu^{64} into ceruloplasmin in one of these patients may still suggest the presence of an abnormality in the metabolism or function of ceruloplasmin.

The nature of the basic defect in hepatolenticular degeneration remains uncertain. There is a wide variation of both the clinical and metabolic findings. Are these all secondary changes, and is the primary expression of the basic defect still undiscovered? Or do these variations represent a series of similar syndromes produced by a series of alleles varying among themselves? These are open questions requiring further investigation and especially more detailed family studies, including families with consanguineous parentage.

Iproniazid in Old Age: Effects on Anginal Pain, Arterial Hypertension and General Conditions. M. C. Lascalea and H. E. Mosso. Rev. Asoc. méd. argent. 73:336-339 (Sept.) 1959 (In Spanish) [Buenos Aires].

Nineteen patients of both sexes, between the ages of 60 and 82 years, with arteriosclerosis, moderate hypertension, and severe angina pectoris were treated with iproniazid. The drug was given by mouth in daily doses which varied between 100 and 200 mg. for a period of time which ranged from 2 weeks to 2 months. Anginal pain was controlled in the majority of the cases, but the drug did not change the course of the coronary disease in any patient. Moreover, it caused hypotension in the majority of the patients, with asthenia, fainting, dizziness, and in some cases shock. By comparing the effects of the drug in the elderly with those in 17 patients with angina pectoris under 60, who received the same dosage, the authors conclude that iproniazid is poorly tolerated by the elderly. They caution against its use for older patients.

The Interrelationship Between Coronary and Cerebral Atherosclerosis: An Epidemiologic, Statistical Study. V. Noseda and L. Croce. Minerva med. 50:2918-2920 (Sept. 15) 1959 (In Italian) [Turin, Italy].

Epidemiologic and physiopathological correlation between coronary and cerebral atherosclerosis was studied in 738 men and 114 women who died of coronary atherosclerosis. The arteries were examined macroscopically in all instances and microscopically in some. Atherosclerotic lesions were divided into mild and severe varieties. The presence of both types of atherosclerosis, coronary and cerebral, was observed in 444 patients (52.1%); it was relatively more frequent among women (87 instances—76.5%) than among men (355 instances—48.4%). The highest incidence of both lesions was observed in the 7th decade of life among men and in the 8th decade among women.

Severe coronary atherosclerosis occurred more often than did the mild variety among both men and women of different ages. Severe cerebral atherosclerosis showed a gradual increase in incidence with age in both men and women; the mild variety had its highest incidence in the 5th and 6th decades of life and then gradually decreased with age. The authors conclude that there seemed to be no unique relationship in the incidence between coronary and cerebral atherosclerosis in this group of patients. Coronary and cerebral atherosclerosis had a differing incidence with advancement of age, because it seems that each variety is subject to its own peculiar anatomic and functional features.

Epidemic Neuromyasthenia. J. F. Fraumeni. South. M. J. 52:1192-1197 (Oct.) 1959 [Birmingham, Ala.].

The author calls attention to an illness, epidemics of which have appeared in many countries during the past decade, and which has been described under such terms as Iceland disease, Akureyri disease, benign myalgic encephalomyelitis, benign subacute encephalomyelitis, epidemic vegetative neuritis, Durban mystery disease, acute encephalomyalgia, poliomyelitis-like illness, lymphoreticular encephalomyelopathy, and epidemic neuromyasthenia. Pursuing a stubbornly protracted and relapsing course, the illness has been characterized by multiple diversified symptoms, including fatigue, stiffness of the neck and back, muscular weakness, myalgias, paresthesias, vasomotor instability, gastrointestinal and genitourinary disorders, and emotional disturbances.

The onset is usually insidious, with lassitude, malaise, headache, low-grade fever, pain in the nape and back, aching in the extremities, irritability, and depression. These prodromes ordinarily precede paretic symptoms by 1 to 30 days, but often seem to abate and constitute an abortive illness. Muscular weakness has been reported in most cases, occurring within 30 days after the onset of the illness and lingering from 1 to 3 months. The paresis is flaccid, with a peculiar predilection for a localized group of muscles in some outbreaks. An extremity frequently feels heavy, bulky, or "asleep"; the patient may be unable to grip objects. Except for rare cases of transient paralysis, tendon reflexes are usually normal. Sporadic findings have included anorexia, somnolence, projectile vomiting, upper respiratory infection, cervical adenitis, aching of the teeth and gums, stomatitis, conjunctivitis, photophobia, retroorbital pain, arthralgias, trophic skin changes, rashes, and edema.

Inoculations of animals and tissue cultures of material from blood, nasopharynx, spinal fluid, and feces have failed to isolate an infectious agent. Complement-fixation, agglutination, agglutination-inhibition, and neutralization tests have demonstrated no immune body production against antigens specific for trichinosis, leptospirosis, brucellosis, lymphogranuloma venereum, toxoplasmosis, encephalomyocarditis, lymphocytic choriomeningitis, ECHO viruses, adenoviruses, herpes simplex, rabies, mumps, Q fever, influenza, poliomyelitis, and the arthropod-borne encephalitides. Epidemic neuromyasthenia often strikes explosively within schools or institutions, especially medical and nursing staffs of hospitals, with a curious partiality for student nurses, or else it is epidemic within the general population, where it primarily affects young adults and predominantly women. There is generally a low proportion of patients under 10 years and over 45 years of age. The clinical pattern and the presence of fever and electromyographic abnormalities distinguish the disorder from a psychopathological one.

The author feels that "epidemic neuromyasthenia" is an appropriately descriptive label for this cryptogenic, contagious, benign, yet protracted and debilitating, disease. It emphasizes the "exhaustion" of mind and muscle that underlies the symptom complex. Treatment has been limited to techniques for support and symptomatic relief. The need of further investigative studies is discussed.

Epidemic Nonicteric Viral Hepatitis: A Report of 120 Cases. L. M. Morrison, M. Inouye, R. E. Hoyt and others. Am. J. Gastroenterol. 32:467-476 (Oct.) 1959 [New York].

The authors emphasize the frequent occurrence of the nonjaundiced form of viral hepatitis during epidemics of icteric viral hepatitis, and report on 120 patients observed during an epidemic of icteric viral hepatitis in West Los Angeles in November, 1956. Patients suspected of being affected by viral hepatitis presented symptoms usually associated with the clinical picture of influenza, such as fever, malaise, generalized aching, arthralgia, cough, sore throat, abdominal pain, nausea with vomiting, or gastrointestinal upset. In some patients the presenting symptoms gave the impression of a psychoneurosis. The liver was found to be enlarged in 73 of the 120 patients, and it was tender or painful to deep abdominal palpation in 108. The spleen was enlarged or palpable in 4 patients. The duration of illness in patients who did not have a relapse or develop persistent symptoms was from 1 to 4 weeks, with an average of 2 weeks before complete disappearance of symptoms. The hemagglutination test for viral hepatitis revealed positive findings in 78 of the 120 patients, the thymol turbidity test was positive in 46, and the cephalin flocculation test was positive in 61. Clinical relapses occurred in 15 patients from 1 to 5 months after the acute onset of the illness.

The carrier state of the virus in this disease is of considerable public health importance. If blood is obtained at blood banks during epidemics of viral hepatitis, special attention should be directed to all blood donors for the possibility of detecting carrier states. Abdominal examination of prospective blood donors for a tender or palpable liver at such times should be routine. Wherever possible the hemagglutination test for viral hepatitis should be performed in conjunction with cephalin flocculation and thymol turbidity tests. The hemagglutination test for viral hepatitis, which was employed with *some modification described in the original article*, was found to be a valuable screening and diagnostic test, which may have specificity for both infectious and homologous serum varieties of viral hepatitis.

Lymphogranulomatosis: Study of Cases. R. Cabrera Madrid. Rev. clín. españ. 73:185-189 (May 15) (In Spanish) [Madrid].

Thirty-two patients with a clinical diagnosis of malignant lymphogranulomatosis were observed in the clinic of medical pathology of the University of Seville; there were 9 women and 23 men, between the ages of 30 and 50 years. The disease was chronic, with repeated acute crises in 29 patients and constantly acute ones in 3. The types of the disease were cervicothoracic in 20 patients, visceral in 4, and either diffuse or in unusual localizations in 8. A biopsy of one or more lymph nodes was performed on 27 patients. The results confirmed the clinical diagnosis in 11 patients, and showed active lymphoid hyperplasia in 6, reticular hyperplasia in 1, and either a normal condition or any of the various pathological changes of the lymph nodes in 9. One patient suffered from "tumoral spleen," a form in which the disease is restricted to the spleen. In another patient biopsy specimens from 3 different lymph nodes showed active lymphoid hyperplasia, tuberculous adenitis, and lymphoblastoma in the first, second, and third lymph nodes respectively. There was severe hypochromic anemia in 31 patients, leukocytosis and lymphopenia in 28, and eosinophilia in 12.

The treatment consisted of roentgenotherapy in association with the administration of nitrogen mustard. Epinephrine and blood transfusions were given during the acute crises. The average survival of the patients from the start of treatment was 2½ years. The survival period was much shorter in a few who were treated with triethylene melamine (TEM) alone. The author believes that malignant lymphogranulomatosis is a special type of reticulosis which progresses to reticuloendothelioma and is often associated with infections, especially tuberculosis of the lymph nodes.

Vitamin B_{12} and the Malabsorption Syndrome. G. A. Goldsmith, F. M. Hunter, A. L. Prevatt and W. G. Unglaub. Am. J. Gastroenterol. 32:453-466 (Oct.) 1959 [New York].

The authors report on 21 patients, ranging in age from 53 to 85 years, who were found to have malabsorption of vitamin B_{12} not corrected by administration of the intrinsic factor. A macrocytic anemia was present in all the patients, and the bone marrow was megaloblastic in all but 3. Serum concentration of vitamin B_{12} was low in 11 of the 21 patients, in whom it was measured during a hematological relapse. Malabsorption of vitamin B_{12}, detected by means of the Schilling test, was present in all the patients. The clinical diagnosis in these patients prior to measurement of the absorption of vitamin B_{12} had been pernicious anemia, nutritional macrocytic anemia, or sprue. Most of the 21 subjects who were found to have malabsorption of vitamin B_{12} had evidence of malabsorption of other nutrients, including glucose, fat, and fat-soluble vitamins.

In every instance, satisfactory hematological response followed oral administration of vitamin B_{12} in doses of 1 to 3 mg. once weekly. Folic acid given in doses of 5 mg. daily has also maintained hematological remission in a number of these patients, but some showed further improvement when vitamin B_{12} was added to the therapeutic regimen. A relapse occurred in several patients in whom therapy with vitamin B_{12} was discontinued; this suggests that malabsorption of vitamin B_{12} may be a permanent defect. It is concluded that therapy with vitamin B_{12} results not only in a hematological remission but also in restoration of a good state of nutritional health, even though absorptive defects of several nutrients may persist.

Leukemia and Exposure to X-Ray: A Report of 6 Cases. W. C. Moloney. Blood 14:1137-1142 (Oct.) 1959 [New York].

The author reports on 2 men and 4 women, between the ages of 38 and 66 years, in whom leukemia occurred after exposure to varying doses of roentgen rays. After the removal of malignant testicular tumors, the men received a dose of 5,200 r directed to the paravertebral lymph nodes and 12,300 r directed to the vertebral marrow respectively. Of the 4 women, one received x-ray therapy first after the removal of a benign breast tumor, and 17 years later she was given x-ray therapy for bursitis and arthritis involving the cervical vertebrae; an accurate estimation of the radiation dose was impossible, but she probably received a minimum dose of 2,000 r and most of it to the chest and cervical areas. The second woman received a dose of 1,600 r to the pelvis and abdomen for bleeding uterine fibroids. The third woman received 2,250 r directed to the chest area on the left after radical mastectomy for cancer of the breast. The fourth woman had pulmonary tuberculosis and received weekly refills of a bilateral pneumothorax under direct chest fluoroscopy over a period of 5 years, and she also had a large number of diagnostic chest roentgenograms; accurate estimation of the dose of ionizing radiation was difficult, but the patient may have received as much as 2,000 r.

Latent periods before the development of leukemia in these patients were variable and difficult to estimate accurately, but the latent periods in radiation-induced leukemia usually vary from 3 to 10 years. In all 6 patients the leukemia was acute; 4 patients had granulocytic, 1 monocytic, and 1 lymphocytic leukemia. The disease began with a pancytopenic onset, simulating aplastic anemia in 4 patients, and in 3 of these the diagnosis was established only after bone marrow aspiration or biopsy.

In man, an understanding of radiation-induced leukemia will be achieved only by acquisition of much more well-documented information, not only of the clinical and hematological findings but especially in regard to the dosage and characteristics of the radiation exposure. In the present state of knowledge, whether or not the evidence can be accepted as valid, it is important that all cases of leukemia attributed to ionizing radiation should be reported in as complete detail as possible.

Some Problems in Diagnosis and Treatment of Hemophilia. B. A. Waaler. Tidsskr. norske lægefor. 79:1111-1118 (Oct. 1) 1959 (In Norwegian) [Oslo].

Estimation of whole blood clotting time is an insensitive test of the function of intrinsic blood coagulation, with many sources of error. If it gives prolonged time, the information is valuable. If the time is not prolonged, diagnosis of hemophilia is not excluded. Estimation of secondary bleeding time is a better test than examination of the whole blood clotting time. Hemophilia can occur in mild degree. The key to the diagnosis of mild hemophilia lies in the patient's history. Special attention should be paid to the bleeding tendency after tooth extraction, injuries, or operative interventions. If transfusion is to be given to a bleeding hemophiliac, the quantity of blood, plasma, or concentrated preparation should be sufficient to raise the level of the antihemophilic factor in the patient's plasma to 15 to 20% of the normal. The effect of a transfusion quickly ends and is almost completely eliminated after 24 hours.

Recent Observations on Porphyria. J. Waldenström. Nord. med. 62:1443-1447 (Oct. 1) 1959 (In Swedish) [Stockholm].

The 2 most important porphyrias are acute intermittent porphyria, with dominant inheritance, of which 494 cases are known in Sweden, and porphyria cutanea tarda. Barbiturates play an important part in precipitating the severe attacks of acute porphyria, fatal in 50 to 60% of the cases. Many of those affected know that they have the "family sickness." It appears that the mortality can now be reduced to a minimum, with attention given to the risk in narcotics. Porphyria cutanea tarda is characterized by special cutaneous symptoms precipitated mainly by the excessive use of alcohol. Both forms represent a genetically determined enzyme defect—"inborn error of metabolism"—which manifests itself under the influence of specific toxic substances. The 2 forms do not occur mixed in a family; each family represents typical biochemical and clinical symptoms.

SURGERY

Maintenance of the Heart Beat by Perfusion of the Coronary Circulation with Gaseous Oxygen. D. C. Sabiston Jr., J. L. Talbert, L. H. Riley Jr. and A. Blalock. Ann. Surg. 150:361-370 (Sept.) 1959 [Philadelphia].

This report is concerned with a group of experiments designed to evaluate the effect of perfusion of the dog heart with gaseous oxygen. Observations have been made both on the isolated heart and on the heart remaining intact within the chest. It was demonstrated that the beat of the isolated dog heart may be maintained for periods of up to 8 hours by perfusion of the coronary circulation with oxygen in the gaseous state. In some instances electrocardiographic activity continued after cessation of visible ventricular contraction and was observed for periods of up to 4 hours after the last visible beat. Perfusion of the heart in situ within the chest with oxygen has been performed, with later reversion to blood and reestablishment of the normal circulation. The studies indicate that oxygen perfused in the gaseous state is utilized by the heart and that cardiac contraction may be maintained for prolonged periods when the heart is perfused with oxygen alone.

Cranial Dermoid and Epidermoid Tumors. J. F. R. Fleming and E. H. Botterell. Surg. Gynec. & Obst. 109:403-411 (Oct.) 1959 [Chicago].

The authors report on 27 patients with dermoid and epidermoid tumors of the skull and brain, who were operated on at the Toronto General Hospital between 1929 and 1956. The tumors of these patients represent an incidence of slightly less than

1% of all the verified brain tumors observed during this period. All except 2 of these patients were adults. Of the 27 tumors, 9 were dermoid and 18 epidermoid. Of the 9 dermoid tumors, 3 were intracranial, 4 were cranial or extracranial (with no displacement of dura), and 2 were lateral orbital. Of the 18 epidermoid tumors, 15 were intracranial, 1 was parietal, and 2 were lateral orbital. These data show that epidermoid occurred twice as frequently as dermoid tumors. The epidermoid tumors had a tendency to occur in lateral locations, while dermoid tumors were more commonly situated in the midline.

Headaches occurred in more than 50% of the patients. Papilledema was noted in only 2 patients, a fact which emphasizes the extreme slowness with which these tumors expand, thus allowing for compensatory cerebral compression and atrophy without great increase in intracranial pressure. Focal neurological signs were much more common. These varied according to the location of the tumor, from visual field changes, epilepsy, and hemiplegia to cranial nerve lesions and cerebellar signs. Proptosis was an invariable occurrence in those anterior temporal and frontal epidermoids that invaded the orbit. The age of onset of symptoms was between 15 and 40 years in most of the patients, and the duration of symptoms before the diagnosis was made was several years. There were 2 operative deaths, one of a patient with an epidermoid tumor in the 4th ventricle, and the other of a patient with a suprasellar dermoid tumor. Signs of recurrence developed in only one patient. Eleven patients are well at the present time. One patient who had a large intratemporal cholesteatoma removed 24 years ago is still alive and quite well. Three patients with suprasellar dermoids or epidermoids are still well, without signs of recurrence, 13, 11, and 10 years after surgical intervention.

Although dermoid and epidermoid tumors of the skull and brain probably arise from a developmental defect in early intrauterine life, they may not produce symptoms until the 3rd or 4th decade or even later. Dermoid and epidermoid tumors are benign and very slow growing, and often have a history of several years' duration. They are curable by complete removal, and a plea is made for early diagnosis. Even if the tumor has spread extensively and total removal is impossible, incomplete removal may render the patient symptom-free for a great many years.

The Late Prognosis in Severe Head Injuries. E. Akerlund. Acta chir. scandinav. 117:275-277 (no. 4) 1959 (In English) [Stockholm].

A late recovery and restoration of working ability were followed up in 26 persons who had survived head injury. Twenty-one persons were involved in motor-car accidents. Fracture of the skull was demonstrated in 19 instances. The trauma affected the dura mater in one patient. At follow-up 1 to 6 years after the accident, 8 of the patients, who were under 24 years of age, had fully recovered, and their working ability had been restored. Eight patients performed approximately the same type of work as before the accident, but they had the following sequelae in varying degree: headache, dizziness, easy fatigability, impairment of memory, and occasional speech difficulty. Ten patients had a diminished working ability.

Post-traumatic epilepsy was the main cause of disability in 4 patients, and was one of the causes in 2. Impairment of sight, hearing, or smell, unstable body balance, hemiparesis, or tremor was the main disabling sequel in 2 patients, and was one of the causes in 4. Satisfactory restitution took place in most patients (about two-thirds) in whom head injury entailed unconsciousness for periods of up to 4 weeks. Severe residual defects developed in patients whose state of unconsciousness lasted longer.

Studies of Recurrent Herpes Simplex Infections Following Section of the Trigeminal Nerve. S. A. Ellison, C. A. Carton and H. M. Rose. J. Infect. Dis. 105:161-167 (Sept.-Oct.) 1959 [Chicago].

The authors report on 26 patients with intractable trigeminal neuralgia, who underwent section of the trigeminal nerve as a therapeutic procedure at the neurological institute of the Columbia-Presbyterian Medical Center in New York. Recurrent herpes simplex, involving only those cutaneous or mucosal areas which had been deprived of sensory nerve supply, developed in 18 of the 26 patients. Virus was isolated from the peripheral lesions of 8 of 12 of these patients, but was not isolated from 2 specimens of the gasserian ganglion. All 26 patients had antibodies which were detected by one or both of the serologic tests used. No significant differences in the titers of neutralizing or complement-fixing antibodies were observed between those patients in whom herpes developed and those in whom it did not. The changes occurring in antibody level after the appearance of the postoperative herpetic infection were irregular. In 4 of 5 patients, in whom preoperative antibody levels could be compared with the titers 5 or more days after herpes appeared, there was no change as measured by the complement-fixation test. In 2 patients there was no change in the titer of neutralizing antibodies. In one patient there was an initial decrease and a subsequent rise. In only 2 patients was an increase in neutralizing antibody observed. These observations show clearly the trivial role of antibody on recurrent herpetic infections. There was no apparent correlation between the severity of the recurrent herpetic infection and the preoperative antibody level.

Myocardial Function After Elective Cardiac Arrest During Hypothermia. T. Cooper, V. L. Willman, P. Zafiracopoulos and C. R. Hanlon. Surg. Gynec. & Obst. 109:423-426 (Oct.) 1959 [Chicago].

The authors studied left ventricular function of dogs which underwent elective cardiac arrest after their temperatures were cooled to between 27 and 30 C (80.6 and 86 F), in comparison with left ventricular function of dogs which were similarly tested at 37 C (98.6 F). Left ventricular function curves were constructed from measurements which were obtained of cardiac output, heart rate, mean arterial blood pressure, and mean left atrial pressures. The results showed that the canine heart, arrested with 2.5% potassium citrate in whole blood in the usual manner at 28 C (82.4 F), is able to perform more than 15 gram-meters of stroke work in response to trial transfusion after the arrest. In contrast, the heart of a dog of comparable size which is arrested at 37 C (98.6 F) is unable to exceed 8 gram-meters of stroke work during the period after arrest. These results indicate that hypothermia offers partial protection to the canine myocardium subjected to 30 minutes of arrest with potassium citrate. The findings support the concept that primary myocardial weakness or failure may contribute significantly to the postoperative morbidity and mortality in those patients who undergo elective chemical cardiac arrest.

Gastrocnemius-Muscle Recession (Silfverskiold Operation) for Spastic Equinus Deformity in Cerebral Palsy. C. M. Silver and S. D. Simon. J. Bone & Joint Surg. 41:1021-1028 (Sept.) 1959 [Boston].

The Silfverskiold operation is a procedure for correction of spastic equinus deformity. This is the commonest deformity of the lower extremity in children with cerebral palsy, and for centuries it has been treated by tenotomy of the Achilles tendon, with disappointing results. In the Silfverskiold operation a transverse incision is made in the popliteal crease, and through it the 2 heads of the gastrocnemius muscle are freed from their attachment to the medial and lateral condyles of the femur. In order to weaken the muscle further, the tibial nerve is exposed, and about half of the motor branches to the 2 gastrocnemius heads are divided; the main tibial trunk, the peroneal nerve, and the popliteal veins must be protected.

The Silfverskiold operation, consisting of muscle "recession" with partial neurectomy, was performed in 110 instances, between 1947 and 1958, on 66 children. It is considered the most reliable and effective procedure when the proper indications are present. Forty-four children underwent bilateral and 22 unilateral operations. Seventeen children had hemiplegia, 10 diplegia, 3 triplegia, and 36 quadriplegia. Thirty-one of the children in this series were unable to walk at the time of surgery, whereas 12 could walk with support and 23 could walk independently. Of the 31 children who were unable to walk at the time of operation, 20 were 4 years of age or older. The average age at the time of operation was 5 years, with a range of 19 months to 13 years. The postoperative follow-up period ranged from 1 to 9 years, but none of the cases can be considered as end-results in the evaluation of correction of spastic equinus until the child has reached 13 years of age, when full growth of the lower extremity has been practically attained.

Five failures occurred in this series of 110 gastrocnemius-recession operations. All of these were apparent within 2 years after the operation. In each instance failure was due to weakness of the dorsiflexor muscles of the foot, which was not properly evaluated before operation. These failures do not reflect on the merits of the Silfverskiold operation. The dorsiflexor power should be tested repeatedly to make sure that the results are accurate. Electrical stimulation might well be a valuable adjunct for muscle testing. It is essential that fairly good power be present in the dorsiflexor muscles of the foot; otherwise the gastrocnemius-recession operation will produce only a temporary correction. In such cases, the treatment of choice is passive maintenance of the foot at a right angle with a drop-foot brace until a satisfactory age is reached for stabilization of the foot by arthrodesis.

Complications in 430 Consecutive Pulmonary Resections for Tuberculosis. R. D. Floyd, W. F. Hollister and W. C. Sealy. Surg. Gynec. & Obst. 109:467-472 (Oct.) 1959 [Chicago].

The authors report on 430 patients with pulmonary tuberculosis, who underwent pulmonary resections at the North Carolina Sanatorium, in McCain, between 1952 and 1957. There were 10 operative and postoperative deaths among the 430 patients, representing a death rate of 2.3% for pulmonary resection over the 6-year period. The death rate in the first 215 patients operated on before the advent of dependable antibiotic agents was 3.7%; it decreased in the second 215 patients to 0.9%. All deaths occurred during the first 2 weeks after the operation, except one which followed hemorrhage during operation. The causes of death were varied and were not peculiar to this category of patients. Eighty-one significant complications occurred. A bronchopleural fistula was the commonest complication and appeared in 45 patients (10.5%). Nontuberculous empyema was associated with fistulas in 6 patients. Hemothorax developed in 18 patients (4.2%). Spread of tuberculous infection occurred in 6 of the first 215 patients. The minimal occurrence of nontuberculous empyema, spread of tuberculosis, and pyogenic wound infection and the disappearance of tuberculous emypema were considered to be directly related to chemotherapy.

The causes of the morbidity and mortality in this series of patients could rarely be traced to patient selection or to a surgical error. Most of the bronchopleural fistulas were treated either by thoracoplasty or by conservative measures determined largely by the clinical progress, associated infection, and size of the fistulous space. Postoperative hemothorax was treated in several ways, such as by streptokinase-streptodornase (Varidase) injections, repeated thoracentesis, decortication, operative evacuation, and observation. The size and distribution of the clot were the principal factors in determining whether or not a closed or an operative method of treatment should be carried out.

Direct Approach to Vertebral Bodies in the Treatment of Tuberculous Spondylitis. J. V. Araujo. Bol. clín. hosp. civis Lisboa 23:209-236 (March) 1959 (In Portuguese) [Lisbon].

Sixteen patients with tuberculous spondylitis were treated surgically by a direct approach to the vertebral body or bodies involved, at the department of orthopedics and traumatology of Hospitais Civis in Lisbon. There were 9 male and 7 female patients in this series, with ages ranging from 16 to 41 years. The spondylitis was lumbar in 6 patients, thoracic in 5, thoracolumbar in 3, cervicothoracic in 1, and lumbosacral in 1. It was complicated by an abscess in 5 patients, paraplegia in 3, nerve compression syndrome in 3, pulmonary tuberculosis in 1, renal tuberculosis in 1, tuberculous meningitis in 1, and paraparesis in 1. All the patients received specific preoperative treatment for at least one month, with isoniazid in the daily dose of 10 mg. per kilogram of body weight combined with 1 Gm. of streptomycin. The operation was performed under anesthesia with tracheal intubation.

The surgical technique in the patients with abscess consisted of incising the abscess, draining the cavity, curetting, and resecting the bone wall. If there was no abscess, the vertebral body was curetted, with removal of all residue and necrotic remnants in the disks. Whenever possible, complete excision of the disk was performed. Once the focus had been removed, the cavity was tamponed with Spongostan containing 1 Gm. of streptomycin and 1 or 2 ampuls of isoniazid. The cavity was also filled with spongy bone taken from a resected rib, or with a graft from a bone bank. The muscular planes and the skin were sutured without drainage.

A follow-up study made within a year after the first patient had been operated on showed that 8 patients had achieved clinical recovery with complete function of the bones, normal sedimentation rate, and normal and painless ability to work. In 5 patients the clinical recovery consisted of partial fusion with recalcification of the vertebral bodies, normal sedimentation rate, and normal function of the bone, although the working ability was limited. One patient was in the process of recovering, with stabilization of the vertebral lesions, restricted and painful functional capacity, and limited work capacity. The remaining 2 patients had been operated on too recently for evaluation of the results. The author recommends this technique for its possibility of simultaneous treatment at different levels, including general therapy, removal of the infectious foci, and complete treatment of the abscesses.

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The Prognostic Significance of Electrolyte and Weight Studies in Congenital Hypertrophic Pyloric Stenosis. N. L. Terezis, W. K. Sieber and W. B. Kiesewetter. Surg. Gynec. & Obst. 109:482-486 (Oct.) 1959 [Chicago].

The authors report on 349 consecutive cases of congenital hypertrophic pyloric stenosis in infants who were treated by pyloromyotomy at the Children's Hospital of Pittsburgh between 1947 and 1957. There were 3 postoperative deaths among the 349 infants, a 0.9% mortality rate. Vomiting, the first and most important symptom of pyloric stenosis, began between the ages of 2 and 4 weeks in 44% of the infants. Onset of vomiting before this age was not uncommon, since vomiting began between the 1st and 14th days of life in 31% of the infants. Ninety-eight (28%) of the 349 infants lost significant weight preoperatively, and 251 (72%) did not. Among those who lost weight, there were 47 who vomited postoperatively, an incidence of 48%. The incidence of vomiting among nonweight losers was 13%. There were 95 patients with alkalosis in the total series; of these, 42 (44%) vomited postoperatively. The incidence of vomiting among the patients without alkalosis was 9%. These data show that, if a patient has preoperative weight loss greater than 227 Gm. (½ lb.) or alkalosis, his chances of having postoperative emesis are 3 to 8 times greater than those of a patient without these aberrations. Duration of surgical intervention seemed to have a bearing on postoperative vomiting, since the incidence of vomiting was twice as great in those patients whose operations required more than 45 minutes as it was in those whose operations took less than 30 minutes.

Total Gastrectomy in Carcinoma of the Stomach. A. Zacho and K. Fischermann. Acta chir. scandinav. 117:278-294 (no. 4) 1959 (In English) [Stockholm].

The authors report on 358 poor-risk patients with gastric carcinoma, who were referred to the Finsen Institute in Copenhagen from other Danish hospitals. Of 143 patients with operable disease, 58 (40.6%) underwent total gastrectomy. The central part of the stomach was in most instances the presumed origin of the tumor. Adenocarcinoma and solid carcinoma were the most frequent types observed. The authors have been more reserved about performing total gastrectomy during recent years than they were 10 years ago, because the benefit of the radical operation seemed to be more than offset by a higher mortality rate and poorer postoperative condition. Thirteen patients were operated on by the abdominal and 45 by the thoracic or thoracoabdominal approach.

Operative or immediate postoperative deaths included 2 among the 22 patients who had radical operation and 10 among the 36 patients who had palliative operation. Mortality was not correlated to the age per se, but to the organic lesions, which are commoner late in life. Atelectases, local inflammation, pneumonia, and size of the tumor were the main factors causing death. The following procedures have been used successively during the past 10 years: esophagojejunostomy, end-to-side, then end-to-end, by the technique of Roux-Herzen; direct esophagoduodenostomy; and interposition of the transverse colon or jejunum between the esophagus and duodenum. The interposition procedure seems to be the most promising.

Cancer of Stomach. O. Noring. Ugesk. laeger *121:1474-1477 (Sept. 24) 1959 (In Danish) [Copenhagen].*

Of 161 patients (108 men and 53 women) with cancer of the stomach, admitted to Central Hospital, Hillerød, Denmark, from 1945 through 1956, 72 were operated on radically. Sixty-three patients were subjected to subtotal gastrectomy, with an operative mortality of 12, and 9 to total gastrectomy, with an operative mortality of 4. Of 46 patients discharged more than 3 years ago, 15 are living, and 31 have died of recurrence or metastases. Eight patients are living 5 years after the operation. Seven of the total 161 patients had had previously, or simultaneously, cancer in other organs, and one patient later had leukemia.

The Postcholecystectomy Syndrome on the Basis of the Late Results in 551 Cases Followed Up During the Years 1950 to 1955. B. Kourias and A. Tobler. Chirurg 30:398-403 (Sept.) 1959 (In German) [Berlin].

After pointing out that according to recent reports the incidence of the postcholecystectomy syndrome ranges from 5 to 30%, the authors recall their own recent report on 36 patients on whom repeat operations had to be performed. These 36 cases constituted 2.51% of a total of 1,432 gallbladder operations. Nearly two-thirds of these second operations were required for retention of calculi in the choledochus; the others were necessary for functional disturbances of the sphincter of Oddi, cicatricial stricture of the papilla of Vater, chronic pancreatitis, stricture of the hepatic and common ducts, disorders caused by long stumps of the cystic duct, aneurysms of the hepatic artery, hepatic echinococcosis, or exploratory purposes.

The present report supplements the earlier one and is concerned chiefly with follow-up studies on 721 patients who underwent gallbladder operations from 1950 to 1955. The investigations were concerned with the incidence and cause of the postcholecystectomy syndrome and with the later fate of the patients operated on. Twenty-six patients (3.5%) died after operation. Efforts were made to trace and reexamine the surviving 695 patients, of whom 483 had undergone cholecystectomy; 170, cholecystectomy plus drainage of the choledochus; 12, cholecystectomy and choledochoduodenostomy; and 30, other operations. Stones were found in 439 (90.9%) of the 483 patients who had been subjected to cholecystectomy. The other 44 patients (9.1%) had disease of the cystic duct or lipoidosis or stasis of the gallbladder. Of the 182 patients in whom choledochotomy was carried out, 123 (67.7%) were found to have lithiasis of the main bile passages.

Follow-up information could be obtained in 551 (or about 80%) of the 695 patients. It was found that the late results were excellent in 388 patients (70.4%) and good in 90 (17.4%); some improvement resulted in 42 (6.5%), and in 31 (5.7%) the results were unfavorable. The authors attribute their favorable results to careful selection for operation, to the systematic use of cholangiography during operation, and to the addition under certain conditions of manometry. Choledochotomy was usually combined with external drainage (170 cases), whereas choledochoduodenostomy was rarely performed (12 cases).

Regarding sphincterotomy, the authors say that, in addition to numerous transduodenal sphincterotomies for impacted stones in the lower half of the choledochus or in the papilla of Vater, they performed only 3 typical sphincterotomies before 1955 for stenosing papillitis or sclerosis of Oddi's sphincter. In the last 3 years, however, they have resorted to it in 10 of 66 choledochotomies. They hope that, with strict selection for this procedure, the results will become even better. Biliary dystonia was not frequent in the patient's operated on, and postoperative sclerotic odditis was rare. External drainage always produced excellent results during choledochostomy.

Cancer of Colon. O. Noring. Ugesk. laeger 121:1477-1481 (Sept. 24) 1959 (In Danish) [Copenhagen].

Of 124 patients (65 men and 59 women), admitted to Central Hospital, Hillerød, Denmark, from 1945 through 1956 with a diagnosis of cancer of the colon, 70 were operated on radically. Operation according to the Bloch-Mikulicz method was performed in 17 cases, with 2 deaths; resection according to Hartmann's method was carried out in 2 cases, and resection with anastomosis, in 24 cases, with 2 deaths; and in 27 cases hemicolectomy with ileotransversostomy or transversosigmoidostomy was performed. The small, stenosing, ileus causing tumors were predominantly in the descending colon; the larger tumors, accompanied by anemia, were mainly in the ascending colon. One-third of the 124 patients were over 70 years of age. Of 44 patients operated on more than 3 years ago, 33 are living, free from recurrence; of 25 operated on more than 5 years ago, 16 are well. Another cancer developed either previously, simultaneously, or later in 7 of the total 124 patients.

Cancer of Rectum. O. Noring. Ugesk. laeger 121:1481-1486 (Sept. 24) 1959 (In Danish) [Copenhagen].

Of 133 patients (83 men and 50 women) with cancer of the rectum, admitted to Central Hospital, Hillerød, Denmark, from 1945 through 1956, 92 were operated on radically. Local excision of papillomatous carcinoma was performed in 13 cases. Abdominosacral operation was carried out in 11 cases; abdominoperineal operation, in 50, and transabdominal resection, in 18; the operative mortality in these 79 cases was 14. Follow-up of the 53 patients operated on more than 3 years ago showed that 32 were living; 21 patients were living 5 years after the operation. Of the total 133 patients, 6 had previously or later another malignant tumor in other organs, and 6 had another cancer simultaneously with the rectal cancer.

Compensatory Mechanisms Following Massive Small Bowel Resection for Intestinal Volvulus D. B. Butler. Surg. Gynec. & Obst. 109:479-481 (Oct.) 1959 [Chicago].

It has been postulated by many workers that after massive resection of the small intestine the body compensates for the loss of a large proportion of its intestinal absorptive surface by various means. Some have suggested that the remaining intestine enlarges, so that there is increased size and thickness with expanded absorptive capacity, that the patient loses weight, so that there is reduced caloric and protein requirement, and finally that probably "intestinalization" of the colon occurs to compensate for the loss of absorptive surface. Others have described patients with massive resection of the small intestine, who ultimately died in marked deficiency status and in whom the remaining segment of that intestine was tremendously dilated and thickened. In the past 8 years the author observed 4 patients with volvulus of the small intestine in whom massive resections of that intestine were required. All 4 patients survived the procedure and were successful in compensating for the loss of a large segment of the small intestine and in maintaining normal nutrition and fluid and electrolyte balance.

One of these patients, a 21-year-old woman, presented a unique opportunity for periodic reexamination of the remaining small intestine and colon to determine whether enlargement or thickening occurred in the small intestine and whether any gross changes occurred in the colon subsequent to massive resection. Seven months after the massive resection of the small intestine, this patient underwent cesarean section because of gross pelvic bony abnormality, and thus the author was offered the opportunity of reexamining the intestine at that time. Measurements revealed the small intestine to be 40½ in. (103 cm.) in length; it was perhaps slightly enlarged in diameter but definitely not in length. The colon appeared normal, with no changes in size, shape, or consistency. One year after this cesarean section, the patient was again delivered by cesarean section, and 2 successive pregnancies were also terminated by cesarean section 3 and 4 years later. Reexamination of the intestines on these occasions revealed that the small intestine was not enlarged in diameter or thickened, and the colon appeared normal in every respect. It thus was demonstrated clearly that successful adjustment may be made by the remaining small intestine after massive resection. The patient failed to exhibit any abnormal absorption mechanism and was successfully carried through 4 pregnancies and 4 celiotomies without any marked alteration in her protein or electrolyte balance. The patient weighs at the present time 5 to 10 lb. (2.3 to 4.6 kg.) more than she did before the original operation.

If massive resection of the small intestine is required, and the remaining segment of that intestine has a normal absorptive capacity, no compensatory mechanism comes into play as long as the small intestine is not overloaded by demands of the body for adequate nutrition or by excessive food intake. At least 50% of the small intestine may be removed in most patients without any marked alteration in their absorptive efficiency.

Abdominal Surgery: Distention of the Intestinal Tract and Postoperative Urinary Retention. M. C. de Motta Maia. Hospital 56:217-225 (Aug.) 1959 (In Portuguese) [Rio de Janeiro].

Intestinal distention and urinary retention are the main postoperative functional disturbances in abdominal surgery; their preventive treatment has become one of the most important concerns of surgeons. In treating 104 patients at the surgical clinic of the Miguel Couto Hospital in Rio de Janeiro, the author used ambenonium (Mytelase), both as a preventive and as a therapeutic, in the treatment of these 2 main complications. The 104 patients in this series underwent various types of surgical intervention for various types of disease. Their ages ranged from 10 to 70 years, with the great majority in the 20-to-60 age group.

To 63 of the patients Mytelase was administered preoperatively in order to inhibit the action of pseudocholinesterase during the 24 hours preceding the operation. The medication was given intramuscularly, in doses of 2 cc. of a 1:16,000 solution every 6 hours. Postoperatively, Mytelase was given as a preventive to 87 patients, beginning 24 hours after the operation. Each patient received an intramuscular injection of 3 cc. every 6 hours, i. e., 4 injections daily, during an average period of 3 to 5 days. As a therapeutic treatment, Mytelase was given to 17 patients who were suffering from postoperative intestinal distention. Most of these had not received any preoperative preventive treatment because of the acute emergency conditions under which they had been hospitalized. To this group Mytelase was administered every 4 or 6 hours, according to the gravity of the complication. In a patient with medullary concussion, the treatment lasted for 12 days and reached a total dose of 144 cc. The results were satisfactory in all cases reported, and the tolerance to the treatment was perfect.

Surgical Treatment of Phlebitis of the Lower Extremities. J. Stalport, E. Nicholas and A. Demelenne. J. Internat. Coll. Surgeons 32:312-323 (Sept.) 1959 [Chicago].

Phlebitis of the lower extremities may be treated in various ways, medically or surgically. Ligation of the internal saphenous vein alone is of some benefit, since it unquestionably prevents the propagation of the accompanying clot toward the femoral vein and its liberation into the venous circulation, which so often leads to pulmonary infarction. Moreover, improvement in the local state of varices often follows this procedure. The operation, however, frequently produces a false sense of security, because it affords the patient no protection against deep phlebitis and the possibility of emboli arising therefrom. This type of ligation may continue to be used, but the patients should be closely watched for signs of deep phlebitis.

Ligation of the superficial femoral vein above its junction with the deep femoral vein, combined with ligation of the internal saphenous vein, safeguards the patient against any significant embolism, provided that it is carried out bilaterally. Operative mortality is practically nonexistent, and sequelae, if present, are very slight as compared with those seen in patients not treated by operation. None of the authors' 95 patients, for whom follow-up was possible, was handicapped in any way as a result of the combined bilateral procedure, although a few had mild edema in the evening and, occasionally, a feeling of heaviness in walking.

The surgical treatment of thrombophlebitis by femoral vein ligation makes the use of anticoagulants unnecessary, and this, in turn, eliminates the undeniable danger of intra-abdominal or juxtacicatricial hemorrhage accompanying the use of these drugs in patients who have been subjected to operations of various kinds. Prophylactic ligation of the femoral veins in patients who are to undergo thrombogenic operations, such as hysterectomy, prostatectomy, or resection of abdominal neoplasms, can legitimately be considered when close observation of the patient is impossible.

Some Epidemiologic Considerations of Thromboembolism. W. W. Coon and F. A. Coller. Surg. Gynec. & Obst. 109:487-501 (Oct.) 1959 [Chicago].

In reviewing the records of 4,391 complete autopsies, performed at the University of Michigan Hospital in Ann Arbor between 1945 and 1954, the authors found pulmonary arterial emboli in 606, an over-all incidence of 13.8%. In an attempt to study the influence of heart disease and cancer, and a combination of both, on the incidence of thromboembolism in the 4,391 patients, the following figures were obtained. The incidence of pulmonary embolism in 1,910 patients with neither cancer nor heart disease was 6%; in 1,135 patients with cancer but without heart disease, it was 14.1%; in 1,087 patients with heart disease but without cancer, it was 22.6%; and in 259 patients having both heart disease and cancer, it was 33.2%. These findings suggested that both cancer and heart disease were factors predisposing to pulmonary embolic complications and that a combination of both factors present in the same patient had a cumulative effect in a further increase in incidence of pulmonary embolism.

Heart disease, cancer, and advancing age were found to have a predominant and interrelated effect on the absolute incidence of pulmonary embolism. On the basis of this epidemiologic information, a program of prophylactic anticoagulant therapy in a selected group of patients with a high predisposition to thromboembolic disease has been proposed as the only rational approach capable of saving the life of patients who will otherwise die of this theoretically preventable complication.

The Concept of Pericardiectomy as a Treatment for Recurrent Idiopathic Pericarditis in the Absence of Cardiac Constriction. H. F. Zinsser, J. Johnson and W. S. Blakemore. Am. J. M. Sc. 238:464-470 (Oct.) 1959 [Philadelphia].

Six patients almost totally disabled by chronic recurrent pericarditis were subjected to pericardiectomy after several attempts at medical therapy. In all these patients the clinical picture comprised severe chest pain, low-grade fever, malaise, grippe-like sensations, and easy fatigability. After a first attack of a more or less marked severity, the patients manifested loss of weight, a leukocytosis ranging from 10,000 to 20,000 cells per cubic millimeter, an increased sedimentation rate, and pleurisy. They were hospitalized for different periods of time, and all suffered relapses as soon as they resumed their normal activities. The pericarditis was a primary recurrent condition, different from the older recognized forms of constriction and tamponade. The diagnosis was made by the clinical history, the finding of a friction rub, and electrocardiographic changes; serial chest roentgenograms revealed changes in the cardiac silhouette.

In all 6 patients pericardiectomy was performed through a sternal splitting, and the pericardium was removed as completely as possible. The postoperative period was uneventful; the patients obtained complete recovery and were in good health at the time this study was made. The authors point out that earlier operation has been the over-all trend in pericardial surgery since the advent of streptomycin, especially in patients with proved tuberculosis for whom the prevention of ultimate constriction is important.

The Controversial Thyroid Nodule: An Appraisal. H. J. Smith. J. M. A. Alabama 29:116-122 (Oct.) 1959 [Montgomery].

The author stresses the following points: 1. The incidence of diagnosed thyroid carcinoma is increasing. 2. Careful study of surgical specimens has shown a high incidence of spread to regional lymph nodes and occasionally transthyroid spread to the opposite lobe. 3. To achieve better end-results in the therapy of thyroid carcinoma, the initial surgery must be more adequate. 4. The alternative to adequate surgery is the complete removal of the primary thyroid malignancy and the control of the metastases by suppression of the thyroid-stimulating hormone. 5. Twenty to 25 years must elapse before a means of treating differentiated thyroid malignancy can be evaluated. 6. Time may ultimately prove that the major factor in curability of thyroid carcinoma is the biological potential of an individual tumor, and that early surgical intervention and the extent of resection of metastatic disease play secondary roles. Until this question is settled, the author prefers to depend upon excisional therapy for thyroid cancer, aimed at the total extirpation of the disease rather than to rest on local excision.

Surgical Treatment of Patent Ductus Arteriosus in Adults. K. Pyörälä, R. Seppälä and E. Laustela. Ann. chir. et gynaec. Fenniae 48:369-389 (no. 3) 1959 (In English) [Helsinki].

Sixty patients (55 females and 5 males) with patent ductus arteriosus, and free from any other congenital or acquired cardiovascular defect, were observed during 1947-1958 at the Hospital of the Wihuri Research Institute or at the Third Medical Clinic, University of Helsinki. The patients' ages ranged from 15 to 48 years, and their most common symptoms were exertional dyspnea, fatigue, and palpitations. In 17 patients the onset of symptoms had been observed after the age of 20, and 2 had been entirely asymptomatic until the development of heart failure. In 37 patients a heart murmur had been detected before the age of 15. Pregnancy and childbirth had been well tolerated by 13 of the women; in only 4 of them the preexisting symptoms had been aggravated during the course of the first pregnancy. Bacterial endocarditis had occurred in 4 patients. A continuous murmur, typical of patent ductus arteriosus, was heard in 57, and in most of these the electrocardiographic findings suggested a left ventricular hypertrophy. Roentgenologic examination revealed a definite enlargement of the heart in 26 patients.

Fifty-six of the patients studied underwent surgical treatment. The severity of the symptoms and the age of the patients were the criteria for deciding on the operation. It was considered that in young persons the potential risks in later life were more serious than the operative risks, whereas in older patients the operation was advisable when the severity of their symptoms outweighed the possible risks of surgical treatment. The 4 patients who had had bacterial endocarditis underwent the operation after an intensive antibiotic treatment and after a complete clinical recovery. The ductus was closed by ligation in 51 patients; it was divided and sutured in 3. A fatal hemorrhage occurred in the remaining 2 patients while the ductus was being dissected and freed from the surrounding tissues.

Forty-eight patients were followed up for periods of from 6 months to 10 years. In 46 the symptoms which were present before the operation had disappeared. The other 2 still had some exertional dyspnea, although they had greatly improved. The heart volume diminished in all the patients with definite preoperative cardiac enlargement and in most of those with preoperative normal heart volume. The authors believe that ligation of the ductus is a safe procedure which gives permanent satisfactory results in most adult patients, but it may be hazardous if there are extensive degenerative changes in the vascular walls. The division-suture method is evidently the only possible surgical treatment when there is a wide or a short ductus.

Pathophysiological Changes During Extracorporeal Circulation: I. Basal Metabolism and Acid-Base Equilibrium. R. Beer, G. Loeschcke, H. Gehl and others. Arch. klin. Chir. 291:443-466 (no. 5) 1959 (In German) [Berlin].

In using the heart-lung machine for open-heart operations, the operative risk is partly dependent on whether and to what extent it is possible to prevent disturbances in the physiological functions. The maintenance of normal conditions with regard to the oxygen and carbon dioxide exchange is of vital importance, and an adequately compensated acid-base economy is another urgent requirement. In their experiments on dogs the authors used the pump-oxygenator of Lillehei-De Wall, and the heart-lung machine of Kay-Gaertner, which is equipped with a film-oxygenator of the Gibbon type. The cardiopulmonary function of the animals was interrupted for from 30 to 40 minutes. Measuring the oxygen intake and the carbon dioxide elimination at various perfusion rates, it was found that above a partial oxygen pressure in the venous blood of 32 mm. Hg, which in the experiments was obtained with a perfusion volume of 35% of the ideal minute volume, the oxygen consumption reached normal values. However, a normal oxygen consumption of the body in general does not necessarily guarantee that an adequate oxygen supply is available to all vital organs.

In a series of experiments with perfusion volumes of 50% of the normal minute volume, in which no carbon dioxide was added to the ventilatory gas in the oxygenator, the blood supply of the brain, on the basis of the lowered blood pressure and arterial carbon dioxide pressure, was only 55% of normal. Under these conditions the venous oxygen pressure in the brain of 25 mm. Hg is within the region of incipient, but still reversible, functional disturbances. After the perfusion experiment, the cerebral circulation was reduced to the same degree, despite the fact that blood pressure and carbon dioxide tension were practically normal; this is interpreted as a sign of increased resistance in the cerebral vessels.

The following are regarded as the causes of the metabolic acidosis that develops during extracorporeal circulation: 1. Acid metabolic products develop as the result of oxygen deficiency, when the perfusion volume is below 35% of the normal minute volume. 2. Fixed acids, particularly lactic acid, are liberated because of the reduced blood pressure. 3. Acid metabolites accumulate as the result of the anesthesia and thoracotomy. 4. There is acidosis in the donor blood as the result of glycolysis. 5. Acid anions develop in the metabolism as the result of induced respiratory alkalosis.

By excluding or compensating for the aforementioned factors by the use of greater perfusion volumes, by avoiding hyperventilation, by storing the donor blood at +4 C (39.2 F), and by compensating for the still existing alkaline deficit by the administration of bicarbonate, it was possible to demonstrate that the extracorporeal circulation as such does not cause a metabolic acidosis. The application of the information derived from animal experiments on the maintenance of physiological conditions in the basal metabolism and in the acid-base economy proved of great value in the extracorporeal circulation and postoperative treatment of patients operated on so far.

Pathophysiological Changes During Extracorporeal Circulation: II. Hemodynamics. H. G. Borst, R. Beer, H. Gehl and others. Arch. klin. Chir. 291:467-481 (no. 5) 1959 (In German) [Berlin].

If heart and lung are replaced by a machine, considerable hemodynamic changes must be expected in the body, because a number of vital regulatory mechanisms are lost. Because there is no longer any automatic adjustment of the circulation to the needs of the body, the minute volume of blood provided by the arterial pump must be adjusted in such a way that the body is furnished an adequate oxygen supply. In order to maintain physiological conditions, the venous suction device must be applied in such a way that a normal venous pressure prevails. The authors evaluate the decisive hemodynamic factors, first theoretically and then on the basis of data determined experimentally.

On the basis of theoretical reasoning, the authors conclude that the quantity of blood in the systemic circulation under the influence of extracorporeal circulation is determined only by the venomotor tonus and by the central venous pressure, and that any change in these 2 factors is reflected in the shifting of blood volume between organism and machine. Surgical blood loss and blood transfusion do not alter the volume of blood in the systemic circulation, but only cause changes in the volume that is in the machine. The total amount of blood in the organism must change, even if during extracorporeal circulation the initial central venous pressure, minute volume, and vasomotor condition can be maintained, because the circulatory bed is reduced by the intrathoracic portion, which is emptied into the machine.

The authors tried to find answers to the following questions in 80 experiments on dogs: 1. What correlation exists between circulatory volume and arterial blood pressure, particularly what volume of perfusion is necessary to hold the blood pressure at least at 70 mm. Hg? 2. At what level should the central venous pressure be maintained to avoid organic damage during and after extracorporeal circulation, and what device is best for regulating venous pressure? 3. What causes blood volume shifts between organism and machine during extracorporeal circulation? 4. When is it necessary to administer vasopressor drugs to counteract the reduced arteriolar or venous tonus?

It was found that blood pressure and perfusion volume are exponentially related; even if the perfusion minute volume is 100% of the basal value, the arterial pressure will not reach normal levels. An average arterial pressure of 70 mm. Hg, which the authors regard as adequate, is achieved with a perfusion volume of from 60 to 75% of the normal minute volume. The authors discuss the advantages and disadvantages of a high minute volume from the viewpoint of hemodynamics. They explain the function of suction drainage to remove the venous backflow with regard to the establishment of a physiological central venous pressure and of the automatic maintenance of this pressure. The blood volume of the systemic circulation adjusts automatically to the value characteristic of the predominating venous pressure, but it changes if, as was observed in experiments, vasomotor-induced changes occur in the circulatory volume. The blood volume in the organism changes during extracorporeal circulation, because its intrathoracic portion does not participate, but is in the machine. Since a tendency to vasodilation exists during extracorporeal circulation, it may be necessary to combat overloading of the organism with blood by the administration of vasopressor agents. The authors stress the importance of the restoration of the initial blood volume, but feel that electronic regulatory devices to maintain a constant blood volume in the machine are of limited value.

Late Results of Surgical Treatment in Patients with Mitral Stenosis. N. V. Putov. Vestnik khir. 83:11-17 (Sept.) 1959 (In Russian) [Leningrad].

The author reports the late results of commissurotomy performed on 91 patients with mitral stenosis. The patients were followed up for a period of from 6 months to 3½ years. Late postoperative results were excellent in 16 patients, good in 44, fair in 20, and poor in 11. Three of the latter patients died. Mitral commissurotomy thus produced excellent and good results in about two-thirds of the patients, but about three-fourths of them required medical assistance or treatment after discharge. Six patients were able to perform physical work without restriction but 6 were completely disabled after the operation; the rest could undertake light physical tasks or nonphysical duties. Of 16 excellent results, 14 were noted in patients under the age of 30 years, and only 2 in older patients. Postoperative complaints, in decreasing order of sequence, were dyspnea (75 instances), pain in the heart area (39), and pain in the liver area (38). The first postoperative satisfactory condition later turned slightly worse in 9 patients and markedly worse in 15. Exacerbation of the underlying rheumatic process was observed in 23 patients among the 31 with fair and poor late results and in 3 patients among the 16 with excellent results.

Complete cure of patients with mitral stenosis after commissurotomy is rare. Mitral commissurotomy may be considered even in instances in which severe pathological changes of the muscle and valves of the heart have taken place. Most of these patients improve after the operation, although excellent results may not be expected. The author believes that a planned medical observation of patients who have undergone mitral commissurotomy is indispensable. The postoperative measures designed to improve the late results of mitral commissurotomy include periodic visits to the public health dispensaries, prophylaxis, and treatment of a possibly exacerbated rheumatic process.

Air Cysts of the Lung. J. R. Massie, J. W. Coxe III, G. A. Welehons and A. G. Bailie. Am. Surgeon 25:737-743 (Oct.) 1959 [Baltimore].

The authors report on 3 men and 2 women, between the ages of 30 and 50 years, with air cysts of the lung. Of these, 1 had an asymptomatic cyst which was found on routine x-ray examination, 2 had air cysts causing symptoms for which they were operated on, and 2 had air cysts complicated by infection for which they were operated on. The patient with the asymptomatic cyst had had yearly physical examinations by an internist, always with normal findings, except for the air cyst revealed by the chest roentgenogram. The week after his latest yearly examination, hemopneumothorax and cerebral air embolism resulted from rupture of the cyst into the pleural space and into a pulmonary vessel during air travel in a nonpressurized plane. The patient died 12 hours later. Although air embolism is a rare complication, its occurrence suggests that probably all bullae should be removed, although asymptomatic, in patients who will be flying in nonpressurized planes. Observations in the other 4 patients operated on showed that, except for patients with infected cysts, local excision of cysts is the method of choice, with emphasis being placed on preserving as much pulmonary tissue as possible. Infected cysts are rare and should not be treated by local or wedge removal because of the possible occurrence of bronchopleural fistula and empyema. Instead, a segmental resection is preferred.

Spontaneous Rupture of the Esophagus Complicating Major Abdominal Surgery. E. A. Gould, P. H. Philbin and H. H. Kerr. Am. Surgeon 25:744-747 (Oct.) 1959 [Baltimore].

The authors report on a 45-year-old woman and a 74-year-old man in whom spontaneous perforation of the esophagus occurred as a complication of major abdominal surgical intervention and was not recognized until autopsy. The woman underwent cholecystectomy and subtotal resection of the body and tail of the pancreas for a large cystadenoma. On the 5th postoperative day the patient suddenly pulled out her nasogastric suction tube and vomited. She immediately went into shock followed by coma, and she died on the 6th postoperative day. Autopsy revealed a 5-cm. linear rupture of the esophagus just proximal to the esophagogastric junction, allowing free discharge of gastric contents into the left pleural space which contained 1,000 cc. of greenish black gastric material. There was 4-cm. esophageal hiatus hernia. Microscopic studies disclosed no evidence of ulcers of the esophagus and confirmed the presence of acute mediastinitis and acute pleuritis on the left. There was no evidence of myocardial or pulmonary infarction. The man underwent multiple colostomies for removal of adenomatous polyps, coloscopy, and revision of a gastrojejunostomy performed 30 years ago for an obstructing duodenal ulcer. Thirty-six hours after the satisfactory surgical intervention, the patient became nauseated and vomited, although his nasogastric suction tube was in place and functioned well. Three hours later he went into shock. Except for oliguria, he responded well to the administration of blood, intravenously given fluids, and pressor agent but continued to sweat profusely. He refused food by mouth and continued to be cold, clammy, and apprehensive. Dyspnea, tachypnea, and cyanosis developed. The temperature rose to 103 F (39.5 C). The patient became comatose and died on the 5th postoperative day. Autopsy revealed a 2-cm. linear rupture of the esophagus, just above the cardia of the stomach, involving the right lateral wall of the esophagus, resulting in an acute mediastinitis, and a small right basal hydrothorax containing 300 cc. of greenish black gastric contents. There was no evidence of pulmonary or coronary infarction. Microscopic examination did not reveal any evidence of esophageal ulcer.

Esophageal rupture in these 2 patients was different in the physical reaction to the catastrophe, as compared with the usual syndrome as it occurs in otherwise healthy persons who have overindulged in food or drink. Neither of the 2 patients complained of severe, agonizing pain beneath the sternum, in the chest and upper abdomen. Both patients went into shock of an extreme type, which was most difficult to manage. Both patients had nasogastric suction with the aid of Levin tubes, and these must be considered in the causation, whether or not they were actual factors. Esophageal rupture followed major, somewhat complicated, surgical procedures which undoubtedly placed extreme demands on the patient's physiological state, and the possibility of stress ulcers must be considered. Both patients refused to take anything by mouth and had cyanosis, sweating, apprenhension, and fever. There were no changes in the electrocardiogram and chest roentgenograms.

It is recommended that for postoperative patients who go into collapse after an attack of vomiting, and whose physical findings, electrocardiograms, and chest roentgenograms do not show any abnormality, one should suspect rupture of the esophagus and obtain an esophagram. On confirmation, the ruptured organ should be repaired by transthoracic approach, the mediastinum opened widely, and the pleural space drained.

NEUROLOGY & PSYCHIATRY

Catamnestic Investigations on 86 Leukotomies: A Contribution to the Surgical Therapy of Mental Diseases. H. L. Bischof. Arch. Psychiat. 199:248-259 (no. 3) 1959 (In German) [Heidelberg].

Although Burckhardt had attempted cortical excision for psychoses as early as 1888, during the present era German neurologists have been restrained in the use of psychosurgery. At the Haar Neurological Clinic near Munich, the first psychosurgical operation was performed in 1946, and so far a total of 131 such operations have been carried out at that clinic on 111 patients. The prefrontal method of Freeman and Watts was employed in 75 operations, and the Fiamberti-Freeman transorbital leukotomy in the remaining 56. All except one patient had schizophrenic disorders. This follow-up study takes account of the 94 patients who were operated on between 1946 and 1957, and in whom more than a year had elapsed since the operation. Since 8 of the 94 patients died, 86 leukotomies remain for analysis.

The results after prefrontal leukotomy were better than after the transorbital operation in that, of those subjected to the first-named operation, 50% could be discharged from the institution and, of those subjected to transorbital treatment, only 35%. Furthermore, 62% of the first group and only 20% of the second group of those discharged were able to resume employment. Leukotomy is justified only for those patients who remain psychotic despite the use of all other available methods. Those "tormented" by frenzy, anxiety, and hallucination not only are most in need of relief, but also were found to respond better than do the ill-tempered, fretful, or peevish patients. The preoperative course of the mental aberration provides important pointers regarding the advisability of leukotomy. The operation is most promising in patients with acute disorders tending toward dementia, but in patients with simple hebephrenia or in catatonic patients who seem to vegetate without tensions leukotomy is not advisable. The operation should be performed relatively early, before the end of the second year. Intensive and individualized psychotherapy largely determines the success of the operation.

Syphilis as a Cause of Mental Deficiency. J. M. Berg and B. H. Kirman. Brit. M. J. 2:400-404 (Sept. 12) 1959 [London].

Among 1,900 patients with mental deficiency, mainly idiot and imbecile children, studied by the authors in the Fountain Hospital in London between 1947 and 1958, there were 12 with a history of syphilis. Eight of these had congenital syphilis, with 3 being classified as taboparetic and 2 as meningovascular, leaving 3 whose mental defect was not certainly attributable to their congenital syphilis. In the remaining 4 patients, the mother only was affected, and there was no proof of infection in the child. The 5 patients with evidence of neurosyphilis in the form of changes in the cerebrospinal fluid, or appropriate clinical signs, represented an incidence of 0.2% of congenital syphilis as a cause of mental deficiency, and even if all 12 patients owed their mental deficiency to congenital syphilis, the incidence in this group would be only 0.6%.

Congenital syphilis is now rare as a cause of mental deficiency in England and Wales. The rise in the incidence of acquired syphilis associated with World War II does not seem to have been paralleled with a great increase in congenital syphilis or mental deficiency due to this cause. This is presumably a result of good antenatal supervision of pregnant women and prompt treatment of acute cases of syphilis among expectant mothers and infants. There is no good evidence that syphilis produces any forms of mental deficiency other than well-recognized syndromes such as dementia paralytica and meningovascular syphilis. Syphilic mental deficiency is eminently preventable and should disappear. So long, however, as the number of adult cases remains at the present still considerable level, it would be unwise to relax precautions; these precautions include routine antenatal Wassermann test or routine investigation of patients admitted to mental deficiency hospitals, with appropriate attention to the families if members with positive reactions are found. Increasing contacts with countries which have been less successful in resolving this problem are an additional argument in favor of retaining such precautions.

Segmental Compression of the Extraspinal Venous Plexus: Its Value for the Diagnosis and Localization of Blocking Lesions of the Spinal Canal: Preliminary Report. O. C. Cruz. Arq. neuropsiquiat. 17:297-300 (Sept.) 1959 (In Portuguese) [São Paulo, Brazil].

A new technique aimed at the localization of blocking processes in the spinal canal is presented. It is to be applied after the condition has been diagnosed by means of Stookey's manometric maneuver (lumbar puncture and use of Strauss's manometer), and consists in compressing hard and long, between the thumb and the index finger, the paravertebral muscles along the intervertebral spaces, going successively from the cervical to the lumbar region. As the venous rings at the level of each vertebra anastomose to one another and form a long venous plexus communicating with the extraspinal system through the intervertebral vein, it is possible to produce small oscillations in the cerebrospinal fluid pressure by increasing the venous pressure in the various segments of the vertebral column. In case of a spinal blockage, the oscillations in the cerebrospinal fluid pressure, caused by the local compression at the intervertebral spaces and registered by a manometer, can indicate with relative accuracy the lower level of the blockage.

The author applied this technique to a group of 5 normal subjects in whom the results of the Stookey manometric test were negative. In none of these subjects did the compression of the spinal muscles at the intervertebral spaces produce any oscillation in the cerebrospinal fluid pressure as registered by Strauss's manometer. The same technique was then applied to a group of 5 patients in whom a blockage of the spinal canal had been diagnosed by Stookey's test. In all these patients the compression of the muscles at the intervertebral spaces below the lower limit of the blocking process caused an increase of 2 to 10 cm. of water in the cerebrospinal fluid pressure. In 4 patients the lower level as determined by this technique was confirmed at an operation oriented by myelography. In view of the value that an accurate localization of a blocking process represents for the surgical treatment of such a condition, the author recommends that this new technique be made a part of the routine examination of all patients in whom a blocking lesion in the spinal canal is suspected.

Meningitis Caused by ECHO 9 Virus: Epidemic with 30 Cases in Ringkjøbing District in 1958. S. Trier. Ugesk. læger **121**:1390-1396 (Sept. 10) 1959 (In Danish) [Copenhagen].

In an epidemic of aseptic meningitis, affecting 30 patients, mostly males, in Ringkjøbing District, Denmark, only 6 patients were over 20 years of age. The initial symptom in most cases suggested bacterial etiology, and some patients showed signs of encephalitis. The cell count in the spinal fluid was substantially higher than that previously considered normal in meningitis due to a virus, and in 12 cases more than 40% of the cells were polynuclear. No bacterial etiology could be established, but enteric cytopathogenic human orphan (ECHO) virus, type 9, was found in 15 cases. The course was benign. Some of the patients were treated with antibiotics, apparently without influencing the course.

Neurological Complications of Antirabic Vaccination. J. L. de Assis and G. H. Duchêne. Arq. neuropsiquiat. **17**:235-250 (Sept.) 1959 (In Portuguese) [São Paulo, Brazil].

The varied neurological manifestations occurring in the neuroparalytic accidents from antirabic vaccination are exemplified in the 11 cases reported. In 8 patients the signs and symptoms indicated medullary involvement. There were specific manifestations of acute diffuse encephalomyelopathy in 4 patients, of acute ascending myelopathy in 2, of acute transverse myelopathy in one, and of myeloradiculopathy in one. Involvement of the spinal cord, of the cranial (especially the optic) nerves, and of the spinal roots was observed in one patient. Exclusive involvement of the peripheral nervous system under the form of the Guillain-Barré syndrome occurred in another patient. In still another patient the characteristic features of acute encephalomyelopathy were confirmed by the autopsy findings. In this patient the lesions had had a delayed onset during a second series of vaccination. The course had been very rapid, and death occurred 11 days after the first symptoms. The authors call attention to the fact that in most cases the neurological picture was preceded by signs and symptoms, such as headache, hyperthermia, and edema of the abdominal wall at the site of the injection, with pruritus, paresthesia, and nausea.

Two therapeutic approaches were used in this series. Eight of the 11 patients were treated with corticotropin (ACTH) administered intravenously and also, in one case, intramuscularly (ACTH-gel). Four of these patients had a complete recovery, and 2 obtained marked general improvement; the 7th patient, who received ACTH-gel intramuscularly, improved only slightly and was left with paralyzing sequels, and the 8th, who had been hospitalized in critical condition, died. The remaining 3 patients of the series were treated with antihistaminic substances (2 with orally and intramuscularly administered Phenergan and one with intramuscularly administered Antistine). All 3 patients recovered completely. The present trend in the management of these neurological complications is the prevention of demyelinization by the use of avianized vaccine.

GYNECOLOGY & OBSTETRICS

Rate, Stage, and Patient Age in Cervical Cancer: An Analysis of Age Specific Discovery Rates for Atypical Hyperplasia, In Situ Cancer, and Invasive Cancer in a Well Population. E. Stern. Cancer **12**:933-937 (Sept.-Oct.) 1959 [Philadelphia].

The use of the Papanicolaou smear for the routine screening of an essentially normal population of women attending the Cancer Detection Center of the Cancer Prevention Society, Los Angeles, made it possible to accumulate data on cervical cancer in such a group. When a comparison was made of the discovery rate, the stage of the disease, and the age distribution of cervical cancer patients before and after the institution of the smear as a standard screening policy, a marked increase in the discovery rate of in situ cancer was found. Although the Papanicolaou technique is not as effective a screening test for invasive cancer as it is for preinvasive cancer, the number of invasive cases discovered can be expected to be adequate, since the visualization of the cervix, together with a thorough history, is included in the comprehensive physical and laboratory examination. The international classification of cervical cancer into stages 1, 2, 3, and 4 has been useful in the selection of treatment method and the measurement of salvage rates, and it provides a basis for comparison of information about the disease on an international scale. Stage 0 has now been incorporated into the international classification of cervical cancer to designate the in situ, preinvasive, or intraepithelial stage.

There were 40,596 patient visits from January, 1955, through June, 1958. Of these, 26,340 were patients examined for the first time. Vaginal pool and direct cervical smears were done initially. In the premenopausal group, appointments were scheduled, so that smears were taken at the midcycle. Repeat studies were done for all women with abnormal bleeding and negative initial smear findings. In the in situ cancer cases staging was verified by the study of cone and total hysterectomy specimens.

Whereas the highest rates for in situ cancer occurred in women between 30 and 49 years of age, those for invasive cancer appeared in those 20 years older. There were 71 stage 0 cancers in women between 20 and 50 years of age, a rate of 4.7 per 1,000 patients, and there were 50 invasive cancer, a rate of 4.4 per 1,000 patients in women ranging in age between 50 and 89 years. Precancerous lesions were most prevalent in the youngest age group. The fact that significant numbers of these lesions persisted after 50 years of age may indicate a basic lesion that is present in significant numbers of women throughout life but is more prominent between the ages of 20 and 49. The drop in the rate of precancerous and preinvasive lesions with age may be related to an etiological factor more prevalent in younger women.

The discovery rates in women who were subjected to repeated tests confirmed the thought that dysplasia precedes stage 0, and stage 0 precedes stage 1, since all but 1 of the 14 cancers discovered in the 11,813 "repeat" women who had had smears previously were stage 0, and of these, 11 were known dysplasias followed as such for at least one year. Only 3 cancers (all stage 0) were found in the approximately 11,000 women with previously negative smears. The low incidence of cancer in the "repeat" population with previously negative smears also illustrates the efficiency of the Papanicolaou smear as a screening procedure for the detection of cancer of the cervix. The differences in discovery rates in special groups of women supported data obtained in earlier studies. Thus, in Negro women the rate per 1,000 patients was 15.2; in American Indian women, 13.3; in Mexican women, 7.2; and in Jewish women, 0.49.

Myomectomy: Clinicostatistical Investigation on Its Long-term Results in Relation to the Genital Functions. P. C. Pozzi and M. Rubbiani. Minerva ginec. 11:676-678 (Aug. 31) 1959 (In Italian) [Turin, Italy].

The occurrence of menstruation and pregnancy after myomectomy was investigated by submitting a questionnaire to 138 women who were operated on from 1945 through 1954. Menstruation continued regularly and painlessly after the operation in 94 women (68.1%). However, the discharges were regular and painful in 18 patients (13.6%), were irregular and painless in 20 (14.3%), and ceased permanently in 2 (1.3%). Myomectomy did not affect significantly the development and course of subsequent pregnancies. Thirty-eight women (27.6%) were pregnant after the operation. Twenty-seven of them had normal labor, 5 had labor with the aid of forceps, and 6 underwent cesarean section. Twins were born in 2 instances—at term in one and during the 7th month of pregnancy in the other. Ninety-one women (65.9%) were not subsequently pregnant after the operation, 5 had abortions, and 4 had pregnancies that terminated in miscarriages. Myomectomy was performed during pregnancy in 8 instances, 6 of which terminated normally and 2 in abortion. The authors conclude that myomectomy may be considered the procedure of choice in all young women with evidence of fibromyoma of the uterus, provided that there is a good chance of preserving the anatomic structure of the uterus close to normal.

Early Therapy with Roentgen Irradiation and Antibiotics for Puerperal Mastitis. P. Mutti. Minerva ginec. 11:669-675 (Aug. 31) 1959 (In Italian) [Turin, Italy].

The author reports on 32 patients with puerperal mastitis among 1,430 hospitalized puerperants. A combined therapy of roentgen irradiation and tetracycline (Achromycin) was given to the patients at an early phase of the disease as soon as pain, hyperemia, swelling of the breast, and fever had appeared. The inflammation appeared in both breasts of 4 patients at different times. One course of roentgenotherapy was given to 21 patients, and 2 courses of treatment to 7. The dose level of one course was 80 r. The irradiated area included the nipple in all instances. A daily dose of 1 Gm. of tetracycline, divided into 4 equal doses, was administered every 6 hours to the patients until the body temperature was restored to normal. The patients continued to nurse their infants uninterruptedly during the treatment.

Complete retrogression of the inflammation before suppuration could develop was obtained between 1 and 4 days after the treatment began. There were no significant changes in the amount of milk secreted, and no sequelae took place. Observation of this series of patients suggests that puerperal mastitis is a disease of epidemic nature and that primiparas contracted the disease more frequently than multiparas. The inflammation developed during the first 10 days of puerperium.

Ovarian Changes Concerned with Gonadotrophic Dysfunction and Associated with Amenorrhoea and Infertility: Treatment by Ovarian Wedge Resection and Eversion with Gilliam Suspension. K. V. Bailey. J. Obst. & Gynaec. Brit. Emp. 66:556-565 (Aug.) 1959 [London].

Bailey continues to treat selected patients with functional amenorrhea by extroversion to the ovaries, a method which he first recommended in 1937. American investigators refer to this condition as the Stein-Leventhal syndrome and treat it by wedge resection of the ovaries. Bailey discusses the range of ovarian changes possible in association with the clinical aspects of this syndrome and its etiology, and he stresses the logical nature of the operation of ovarian eversion combined with Gilliam suspension. Since 1937 he has not changed his initial concepts with regard to the major factor of the association of bilateral polycystic ovaries with the clinical aspect of the syndrome described by Stein and Leventhal. He suggests, however, that the basic gonadotropic dysfunction concerned might result in certain other changes in the ovaries (cirrhosis, cirrhoticocystic change, cystic and cirrhotic atrophy), which are also associated with the clinical symptoms identical with those of the Stein-Leventhal syndrome, and which call for the same surgical treatment, although with the expectancy of less favorable results.

The etiology of this syndrome and the ovarian changes associated with it remain in doubt. The author's view, on which his surgical technique is based, differs somewhat from those of others. Pathologically he recognizes 3 main types of ovarian changes in conjunction with the clinical aspects of this syndrome: (1) polycystic ovaries, which constituted about 80% of his cases; (2) cirrhoticocystic and diffuse cirrhotic ovaries; and (3) cystic and cirrhotic atrophy of the ovaries. These may result from gonadotropic dysfunction initiated *de novo,* or may possibly result by slow retrogressive change from the former type.

Bailey describes the rationale of ovarian eversion combined with Gilliam suspension. All forms of medical and hormonal treatment must first be tried, but it is unwise to unduly prolong medical treatment where there is evidence of no success and where examination discloses the presence of uterine, endometrial, and ovarian changes. Approximately 80% of the author's cases conformed clinically and pathologically to the Stein-Leventhal syndrome. These may be regarded as forming the major part of a clinical hormonal syndrome caused and initiated by the same type of gonadotropic dysfunction, and manifested only by the degree to which this dysfunction is operative in the particular patient.

Histopathology of Striae Gravidarum. L. O. S. Poidevin. J. Obst. & Gynaec. Brit. Emp. 66:654-656 (Aug.) 1959 [London].

The author briefly outlines the evolution of the present-day views on the tissue changes in striae gravidarum and shows that an elastic tissue failure is generally accepted. Many textbooks on obstetrics persist in the view that stretching causes rupture of the elastic tissue fibers, which as a result are not found under the stria but rather all curled up at the edge. The author obtained the consent of pregnant women for the removal of complete striae under local anesthesia. Experience showed that the stria in its full length, breadth, and depth should be removed completely, together with a small area of surrounding skin. Striae were removed from various situations, such as the breasts, abdominal wall, and thigh, at various stages of pregnancy. No evidence of tearing and retraction of elastic fibers from the skin of striae was found. The evidence obtained suggested that striae gravidarum result from ground substance changes which permit a rearrangement, rather than a tearing, of either the collagen or elastic tissues. Associated studies suggested a close relationship between striae gravidarum and adrenal cortical hyperactivity.

Monitoring the Heart of the Foetus and the Newborn. D. J. MacRae. Lancet 2:266-269 (Sept. 5) 1959 [London].

During normal labor the rate and rhythm of the fetal heart alter with uterine contractions, and at engagement of the fetal head. In abnormal labor such changes are common in fetal distress, and not infrequently the first warning of danger to the fetus is the absence of fetal heart-sounds. Unfortunately, with the ordinary fetal stethoscope, long periods elapse without a check being made on the heart, so that fetal distress may be well advanced when first discovered. The author has been trying to discover a means of continuously monitoring the fetal heart. His efforts have been centered on finding a small microphone which could be worn in comfort by the mother, and would transmit fetal heart-sounds without interference. Such a microphone is embodied in the "Soniscope," as described by Kinnier Wilson, Fothergill, and Selwyn Taylor in 1956.

The microphone is placed on the maternal abdomen over the area where the fetal heart is best heard, and the microphone is then connected to the soniscope, which selects and amplifies the fetal heart-sounds, and, by means of earphones, the sounds are tuned to their optimum volume. Another output socket connects up with a loudspeaker. The soniscope can be attached to the foot of the bed or left on a bedside table, and the loudspeaker can be placed in a corner of the labor ward or taken to another room. Continuous monitoring of the fetal heart during labor provides early evidence of fetal distress. Such monitoring is necessary (*a*) in abnormal labor, (*b*) whenever a pitocin drip is being given, (*c*) in the anxious and sleeping patient, and (*d*) in the second stage of labor. The cardiophone permits auscultation of the fetal heart during uterine contraction, giving warning by excessive slowing; it reveals reflex fetal kicks and tumultuous movements of distress; and during forceps delivery it can guide the strength and duration of traction. Where complications are suspected during pregnancy, periodic checks by cardiophone (or phonocardiograph) will reveal any disturbance of fetal heart-action. In the newborn infant the cardiophone provides an important guide to the condition of the heart (*a*) when there has been irregularity of the fetal heart-rate, (*b*) during resuscitation from asphyxia, (*c*) in the presence of recurrent cyanosis, and (*d*) during exchange transfusion.

PEDIATRICS

Treatment of Icterus Neonatorum of Prematurely Born Infants with Kollidon Infusions (Periston N).

J. Dieckhoff, L. Theile and H. Theile. Ztschr. Kinderh. 82:539-547 (no. 5) 1959 (In German) [Berlin].

The authors point out that some investigators recommended the low-molecular kollidon, Periston N, as an adjuvant to exchange transfusion in the treatment of hemolytic jaundice in prematurely born infants, because they had found that after the administration of this synthetic blood substitute the dangerously high bilirubin content of the blood was rapidly lowered by increased secretion in the urine. Periston N is a 6% solution of polyvinylpyrrolidone (kollidon) in isotonic sodium chloride solution, which had been used for blood replacement during World War II. The authors studied the behavior of bilirubin in the blood of prematurely born infants, the influence of single or repeated infusions of colloidal solutions on the bilirubin content and the plasma protein bodies as well as the therapeutic effects. On the basis of their observations they arrived at the following conclusions: 1. In response to a single administration of Periston N the bilirubin content of the serum and the albumins decrease considerably within one hour, whereas after the infusion of sodium chloride solution no such changes become apparent. 2. The change in the plasma proteins is the result of a reversible change in the albumins and is not caused by dilution; the globulins remain practically unchanged. 3. When Periston N is infused repeatedly, the excretion of these colloids is compensated by a return of albumins into the blood stream for the maintenance of the colloid osmotic pressure, and this, in turn, results in the simultaneous return of bilirubin; thus, any therapeutic effect is nullified. 4. The only effective treatment of hyperbilirubinemia in prematurely born infants is exchange transfusion.

Hodgkin's Disease in Children: A Clinicopathological Study of 46 Cases.

J. A. Pitcock, W. C. Bauer and M. H. McGavran. Cancer 12:1043-1051 (Sept.-Oct.) 1959 [Philadelphia].

The prevalent view that the prognosis of Hodgkin's disease in children and adolescents, under 16 years of age, is poor and that the disease tends to run a uniformly fatal and often rapid course induced the authors to investigate this problem. The clinical records of the St. Louis Children's Hospital were reviewed; all the lymph node biopsy material prior to 1954 (minimum follow-up of 5 years) from persons less than 16 years of age was examined; and the autopsy protocols and microsections of children dying of malignant lymphoma were studied. No case was included in which no microsections were available to confirm the diagnosis. Two of the total of 46 patients could not be followed up, but the remaining 44 children and adolescents were followed until they died or up to the time of this investigation.

It was found that Hodgkin's disease in this age group, in contrast to the prevalent view, is not uniformly and rapidly fatal, and thus neither warrants a pessimistic approach in the early stages of the disease nor justifies therapeutic nihilism. Eight patients (17%) are still alive 5 to 33 years after biopsy confirmation. The most important factor relating to prognosis is the clinical stage of the disease at the time of diagnosis. The 5-and-10-year survival rates for patients with stage 1 disease are 60 and 35%, respectively, whereas all stage 3 patients died within 3 years. However, survival also could be correlated with the histological type, and the most accurate evaluation depends upon both features. Initial doses of irradiation therapy of less than 1,800 r, in stage 1 cases, failed to eradicate the disease and necessitated retreatment of the lymph node area in all cases.

Based on the successful outcome of 6 of the 7 stage 1 cases, in which the patients were treated with irradiation in excess of 1,800 r, the authors recommend a therapeutic regimen patterned after that of Peters and Middlemiss and Nice and Stenstrom as a rational approach to the treatment of Hodgkin's disease in children. These authors reported a better than 50% survival of 10 or more years in children with stage 1 Hodgkin's disease, who were treated with doses of 2,500 to 3,000 r. Areas of recrudescence, after adequate therapy to the primary site, should also be vigorously treated, inasmuch as 4 patients (initially stage 1) were treated in this fashion and are still living 10 to 33 years after biopsy. Chemotherapy was used only in the terminal stages of the disease in 5 cases. No case of Hodgkin's disease was encountered in a child less than 2 years of age in this series, and the authors doubt the validity of the diagnosis of Hodgkin's disease in infants. They found evidence for the existence of a peak in incidence at about the age of 6 years.

Neurological Examination of Dystocic Newborn Infants. A. M. Franchini and G. Conca. Minerva pediat. 11:822-825 (Aug. 25) 1959 (In Italian) [Turin, Italy].

The authors made and compared 2 examinations, the neurological and the encephalographic, in 25 at-term newborn infants, aged between 1 and 18 days of life. There was a group of 16 dystocic infants and a control group of 9. Significant pathological changes of the nervous system on neurological examination according to the technique of Andre-Thomas and Saint-Anne Dargassie were observed in 2 of the newborn infants. The encephalograms showed pathological changes of the brain in 8 infants, 4 of whom presented electrogenetic changes in paroxysmal variety and 4 had a generalized slow dysrhythmia. The conclusion is that it is advisable to make the encephalographic examination of all dystocic infants and not just those who are suspected of having a brain lesion. Neurological examination alone is not sufficient to demonstrate the presence of a lesion, or to exclude it with certainty.

Pulmonary Tension Emergencies in Infants. A. Backman, K. V. Parkkulainen and M. Sulamaa. Ann. paediat. Fenniae 5:172-182 (no. 3) 1959 (In English) [Helsinki].

The authors report on 8 infants with tension emphysema, their ages ranging from 2½ to 10½ months, who were observed at the Children's Hospital of the University of Helsinki after 1952. In all 8 patients the clinical picture was dominated by respiratory difficulty which had set in at an early age. Cyanosis was often present, particularly when the baby cried. The symptoms were progressive and often occurred in bouts. Histologically the emphysematous lobes exhibited distended alveoli, ruptured alveolar walls, and in many cases even large cavities. The walls of the cavities were lined either with endothelium or with squamous or cubical epithelium. Radiograms showed an emphysematous pulmonary lobe. The tension was often so marked that the other ipsilateral lobes were atelectatic, and the ipsilateral diaphragm was depressed. The mediastinum was often shifted to the contralateral side. In the emphysematous area the pulmonary structure was often visible, which prevented confusion with tension cysts. Three of the 8 infants, who were treated by resection of the distended segment, made excellent recoveries. The remaining 5 infants died. It is believed that in 3 of them a too conservative attitude toward diagnosis and treatment resulted in failure. In the 4th infant diagnosis was very difficult, and it is doubtful whether surgical treatment would have saved the child. The death of the 5th infant occurred within one day of admission because its condition was too deteriorated.

The etiology of this condition often remains obscure. It is believed that compression by anomalous vessels, weakness of the bronchial cartilages, mucosal folds, local inflammatory processes, and external structures compressing the bronchi are etiological factors. It is emphasized that active surgical intervention, and even emergency treatment, is the only correct treatment as soon as the diagnosis has been confirmed.

Phenylketonuria Treated from Early Infancy. D. Murphy. Irish J. M. Sc. 6:425-427 (Sept.) 1959 [Dublin].

Of the 2 children with phenylketonuria whose histories are presented, the first was a boy, the 10th child in a family, in which 3 sisters had phenylketonuria and were severely retarded. In this boy the ferric chloride test (a few drops of ferric chloride added to a fresh specimen of urine) was found to be positive when he was 6½ weeks old. Treatment with a diet in which the phenylalanine was restricted was started at once, and the boy has received this diet ever since. Now at 3 years of age he is well within the normal range of physical and intellectual development for his age. The second patient was the 11th child of the same family. In this girl the urine was tested daily from birth and became positive on the 11th day. The restricted diet was started on the 14th day and has been given continuously since. The infant has progressed satisfactorily, mentally and physically. Now at 20 months she talks in simple sentences and sings, and she is normal for her age.

These 2 treated children are in striking contrast to the 3 untreated affected siblings. Treatment was started before the elevated serum phenylalanine or its metabolities had done irreversible damage to the developing brain. As the greatest damage appears to be done in the first 6 months, it is essential that treatment be started if possible during the neonatal period. It has been recommended that all newborn infants should have the ferric chloride urine test at 3 weeks and again at 6 to 8 weeks of age. A few drops of ferric chloride solution are added to a fresh specimen of urine. If a green color results, the test is positive. The restricted diet is based on that used by Woolf and associates. Since phenylalanine is present in most dietary proteins, a special hydrolyzed casein prepared by acid hydrolysis and treated with acid-washed activated charcoal is the basis of this diet. The necessary amino acids, tryptophan and tyrosine, removed with the phenylalanine have to be readded. The composition of a convenient preparation for the dietary treatment of phenylketonuria is listed. Because some phenylalanine is necessary for positive nitrogen balance, some milk is given in addition to the preparation. Older children are given vegetables in addition, but not potatoes and legumes, which have a high phenylalanine content.

Empyema in Children. G. van Hooren and H. H. van Gelderen. Maandschr. kindergeneesk. 27:245-257 (Aug.) 1959 (In Dutch) [Leiden, Netherlands].

The authors analyze the results of conservative treatment in 55 children with empyema, who were observed in 2 clinics in The Netherlands from 1955 to 1958. Twenty-eight of the children were less than 1 year old, and 25 of these 28 were less than 6 months old. Only 5 of the children were over 5 years old. Staphylococci were the only bacteria found in the pleural pus. Resistance to penicillin was observed in about half of the children with staphylococcic empyema, and all of them had a history of hospital contact; either the child or members of its family had been in the hospital, or the child had been treated with penicillin at home. Resistance to broad-spectrum antibiotics was rare. A detailed history about hospital and other contacts with staphylococcic infections is of vital importance in children with empyema. Pleural puncture was performed once or several times in 46 of the patients. In view of the tendency to spontaneous absorption of empyema in children, the authors question the need of frequent punctures.

Treatment was largely conservative, and consisted chiefly in the administration of broad-spectrum antibiotics. The administration of these antibiotics must be continued for at least 3 weeks. Thoracentesis is usually unnecessary, and should be resorted to only when pus production is profuse. The intrapleural administration of proteolytic agents, such as Varidase, can usually be dispensed with. In one of the 6 children, in whom the authors used Varidase, a bronchopleural fistula developed. Prolonged hospitalization until all physical signs had disappeared seemed of no particular advantage. Only one of the children died, presumably of widespread bronchopneumonia and cystic fibrosis of the pancreas. The other children recovered completely, except for one child in whom collapse of one upper lobe occurred without clinical signs. The chief complication was tension pneumothorax which occurred in 6 of the children, all of whom responded to closed suction. The belief of some investigators that early drainage is required in most children with empyema is not supported by the fact that good results were obtained with conservative treatment.

Description of a Case of Pitressin Resistant Diabetes Insipidus. R. Bruni and L. Massimo. Minerva pediat. 11:857-869 (Sept. 8) 1959 (In Italian) [Turin, Italy].

The authors report a case of nephrogenic diabetes insipidus in a boy who was hospitalized at the age of 4 years. The child grew normally until the 7th month of life, when he contracted pneumonia. Polyuria and polydipsia developed subsequently, although the body weight remained unchanged until the 15th month of life. The disorder was fairly well managed for 2 years with an extract of the posterior lobe of the pituitary body, but the symptoms worsened over a period of several months before hospitalization. On admission, the child had excessive sodemia, potassemia, increased urinary excretion of sodium, diminished urinary excretion of potassium, and increased urinary ratio of potassium to sodium. There were also observed a considerable degree of polyuria, arrest of body growth, mental retardation, slight changes in the electroencephalograms and electrocardiograms, and oily and slightly inelastic skin of the hands.

The patient was placed on a salt-free and low-protein diet. The diet induced a rapid restoration of serum potassium and sodium levels, improvement in the urinary potassium and sodium excretion levels, and increase in the urinary ratio of potassium to sodium. Diuresis, thirst, and the skin condition became normalized; there was a resumption of body growth; and the electroencephalographic and electrocardiographic patterns returned to the norm. The child became used to his new diet without any apparent disturbance. Although nothing significant in the history of the parents was revealed, test findings of the mother indicated that she was a "carrier."

Acrodynia: Selter-Swift-Feer's Disease, Pink Disease, Dermatopolyneuritis: Review and Case Report. E. Kringlen. Tidsskr. norske laegefor. 79:1061-1063 (Sept. 15) 1959 (In Norwegian) [Oslo].

Acrodynia is a rare, protracted, and troublesome disease. Because of its uncertain etiology and pathogenesis and its often strange symptoms, it has attracted much attention among pediatricians. It usually affects children under 6 years of age, particularly children aged from 6 months to 3 years. The symptoms develop insidiously, with mental changes. The child becomes irritable, is often apathetic, and the sleep rhythm is disturbed. A general hypotonia develops; the head droops forward between the knees, presumably because of atonia and aversion to light. Various exanthems appear, especially on the extremities. The blood pressure is usually raised. The child is afebrile if no secondary infection has set in. Anatomicopathological examinations of different organs have not been illuminating. The long-range prognosis is good. Improvement is slow. The symptoms, as a rule, reach their maximum after a couple of months, and the child is well after 7 or 8 months. Treatment with dimercaprol as soon as possible is recommended. The usual dosage is 2.5 mg. per kilogram of body weight every 4 hours the first 2 days, every 6 hours the third day, then twice daily for 10 days. The sooner the treatment is started, the better the result. Treatment otherwise is symptomatic. In the typical case described, in a girl, aged 1½ years, diapers washed in mercury solution had been used for 4 weeks because of a dermatitis. Pathological mercury values were found in the urine. Injections of dimercaprol brought increased excretion of mercury and caused some clinical improvement. As far as possible, medicaments containing mercury should be avoided in infants and young children.

UROLOGY

Retropubic Extravesical Prostatectomy: Clinical Experiences in Over 1,000 Cases. H. Klosterhalfen. Chirurg 30:419-420 (Sept.) 1959 (In German) [Berlin].

The 1,000 retropubic extravesical prostatectomies were performed at the urologic institute of a clinic in Düsseldorf during the years from 1948 to 1959. A total of 1,331 patients with prostatic enlargement causing severe disturbances in urination were admitted during the period in question. A radical operation was considered inadvisable in 119 of these patients, and 212 patients were subjected to electroresection. Carcinoma of the prostate existed in 226 of the patients, but in 44 patients the malignant nature of the lesion was recognized only at operation.

Operability of patients with enlargement of the prostate is determined by the patient's cardiac and renal function. While a considerable number of patients may be inoperable when they arrive at the clinic, the renal function can usually be restored to a point that surgical treatment will be possible. The number of patients in whom renal disorders make surgical treatment impossible is small compared with the number in whom cardiovascular and pulmonary disorders prevent surgical treatment.

Potentiated peridural anesthesia was employed in all the patients, because it not only facilitates circulatory stabilization during and after operation, but also early rising for the patient who is threatened by embolism. Furthermore, blood loss is lessened, because the systolic blood pressure is reduced. The author resorts to the use of anticoagulants only for therapeutic (thrombosis or infarction), but not for prophylactic, purposes. Hypertension is not a contraindication to surgical treatment; at any rate patients with hypertension were not bothered by late bleeding, but 4 of 115 suffered apoplectic strokes after prostatectomy. No unusual difficulties were observed in the 21 diabetic patients. Diabetes mellitus is no contraindication to the operation, but the diabetes should be controlled with ordinary insulin.

A postoperative incontinence is usually of short duration. Osteitis pubis is regarded by some as one of the most annoying complications of retropubic prostatectomy, but the author observed this complication in only 9 of the 1,000 patients, and in the last 300 patients it was never observed. Treatment with cortisone derivatives arrested the symptoms in some of the patients. The author stresses the following advantages of the retropubic extravesical technique of prostatectomy: it provides an excellent survey, facilitates hemostasis, has a low mortality rate, rarely is followed by incontinence or stricture, preserves potency, and combines these advantages with rapid wound healing and short hospitalization.

Carcinoma of the Prostate Gland in a Three-Year-Old Child: Report of a Case. E. H. Kagan and P. G. Fox Jr. Am. J. Clin. Path. 32:261-269 (Sept.) 1959 [Baltimore].

A 3-year-old boy was admitted to the urologic service of the St. Philip Hospital, Richmond, Va., in June, 1958, with acute urinary retention of 12-hour duration, after urgency, frequency, and intermittent retention were observed for 4 days. On rectal examination, an oval, nontender, hard, symmetrical mass, measuring approximately 2 by 3 cm., was palpated in the region of the prostate gland. On the 23rd day of hospitalization, the child was taken to the operating room where, under general anesthesia, a lower midline abdominal incision was made, and the prostate exposed retropubically. Tissue for a biopsy was taken from the prostate, and a frozen section was reported as a malignant tumor of the prostate. A radical retropublic prostatectomy and cystectomy were performed, and the ureters were transplanted to the lower sigmoid. Deep roentgenotherapy was given after the operation. The child remained well for about 6 months. Then a chest film revealed left pleural effusion. A thoracentesis was performed, and the fluid was observed to contain tumor cells. The child's condition rapidly deteriorated, and he died in respiratory distress. There was no local recurrence. Three similar instances have been previously reported, this case being the first in the American literature.

THERAPEUTICS

A Contribution to the Knowledge of the Pathogenetic Mechanism of Acute Hemolytic Anemia Due to Sulfonamides. F. Grignani, P. Brunetti and E. Sulis. Riforma med. 73:1013-1018 (Sept. 5) 1959 (In Italian) [Naples].

The cases of 4 patients who suffered from episodes of acute hemolytic anemia during treatment with sulfonamides are reported. Two of the patients were brothers; the medical history of their immediate family showed that other relatives had suffered from acute hemolysis. The mother of the 2 brothers in her youth suffered from a classical episode of icterohemoglobinuric favism, and since then every spring she was subject to a minor manifestation of intolerance to Viciafava (a kind of bean) pollen. Another member of the family, a brother, died of hemolytic anemia in the neonatal age, and a last member died at the age of 2 while being treated with sulfonamides. A study of the glucose-6-phosphate dehydrogenase erythrocyte activity showed that the enzyme was absent in all members of the family who were examined. The authors believe that there was in the 2 brothers whom they observed a predisposition to hemolysis.

The third patient took sulfonamides because of acute blennorrhagia, and the fourth took one dose only of the drug while suffering from a simple episode of angina. Both patients presented hemolytic manifestations only once. A study of the erythrocytes revealed the absence in both patients of bioenzymatic signs that are found in subjects suffering from favism and other toxicohemolytic anemias. The authors believe that acute hemolytic anemia which occurs during treatment with sulfonamides is characterized by peculiar pathogenetic features that are not found in icterohemoglobinuric favism or in other diseases caused by drugs. This anemia may occur at times because of hypersensitivity to the drug, although no relationship with known erythrocyte biochemical disturbances has been found.

Steroid Therapy in Hirsutism and Virilism. R. R. De Mowbray, A. W. Spence, V. C. Medvei and A. M. Robinson. Brit. M. J. 2:456-459 (Sept. 19) 1959 [London].

The authors report on 8 women with adrenal virilism and a raised 17-ketosteroid excretion, who were treated with a new preparation of prednisolone trimethylacetate (consisting of a microcrystalline suspension of 200 mg. of the hormone in 2 ml. of an aqueous isotonic buffered solution) injected intramuscularly, with prednisolone or prednisone given orally or with an intramuscular injection of hydrocortisone acetate. Intramuscular injections of 400 mg. of prednisolone trimethylacetate at weekly intervals were required to effect suppression of corticotropin, judged by depression of the 17-ketosteroid excretion, whereas daily doses of 20 mg. of prednisone or prednisolone given orally caused an immediate and profound suppression of corticotropin. Two injections of 250 mg. of hydrocortisone acetate given intramuscularly at an interval of one week to a hirsute woman, aged 28 years, resulted in a gradual fall in 17-ketosteroid output from a mean figure of 20.2 mg. per 24 hours before treatment to a level of 8.5 mg. per 24 hours 5 days after the second injection. The output was still slightly below the initial mean figure as long as 43 weeks after the second injection. The same result was achieved in a 26-year-old woman with obesity, amenorrhea, and slight hirsutism, who received an initial intramuscular injection of 250 mg. of hydrocortisone acetate, followed by a second injection of 125 mg. 2 weeks later and a third injection of 250 mg. after a further 2 weeks.

With all 3 methods suppression of adrenocortical function persisted for many weeks or months after withdrawal of therapy. For this reason short intermittent courses of steroid therapy are advocated except in women with pseudohermaphroditism. No significant improvement in hirsutism was obtained in any of the 8 patients, and therefore steroid therapy is not justifiable on the grounds of hirsutism alone. In 2 patients with oligomenorrhea normal menstruation was restored, in 1 patient amenorrhea persisted, and in the remaining patients menstruation was normal before treatment.

The Suppression of the Supervenient Symptoms of Ragweed Pollinosis with Dexamethasone. E. A. Brown. Antibiotic Med. 6:412-420 (July) 1959 [New York].

Of 685 patients with either allergic coryza or bronchial asthma or both, caused by ragweed pollen, who had been treated with a single injection of emulsified extract of the causative allergen, 113 presented symptoms of sensitivity, however transient, during the ragweed pollen season. In 56 of the 113 patients these symptoms could with some certainty have been due to insufficient or imperfect hyposensitization. Of the 56 patients, 31 were men and 25 were women. There was no relationship between the necessity for additional medication and sex, age, nature of disorder (as allergic coryza or bronchial asthma or both), duration of symptoms, degree of skin test sensitivity (or eye test response when present), dose administered, or date of injection. Complete suppression of symptoms was obtained in these 56 patients by treatment with dexamethasone given in doses of 1 mg. every 4 hours for the first day, and, in adults, decreased by the 7th day to 0.5 mg., given 2 or 3 times daily; in adolescents and children, the dose was decreased to maintenance levels by the 4th instead of the 7th day. Fifty-one of the 56 patients needed less than a total dose of 100 tablets of dexamethasone in the 0.5-mg. size. No immediate and no remote ill-effects have been reported or noted.

Dexamethasone Therapy in Bronchial Asthma. J. Duvenci, S. Chodosh and M. S. Segal. Ann. Allergy 17:695-700 (Sept.-Oct.) 1959 [St. Paul].

The authors report on the use of dexamethasone in 41 patients with chronic bronchial asthma for periods of 2 weeks to 7 months. There were 31 women and 10 men, their ages ranging from 24 to 71 years; 63% of the patients were above the age of 50. Thirty-one patients had received either prednisolone or triamcinolone before treatment with dexamethasone was started. The initial dose of dexamethasone varied from one-fourth to one-half by weight of the dose of the previously used triamcinolone. The average maintenance dose required for the control of these asthmatic patients was about 1 mg. daily.

The response to treatment with dexamethasone was considered good in 32 patients and fair in 7. In 2 patients, in whom the drug was withdrawn because of early complications, the response of their bronchial asthma could not be evaluated. A significant observation was the increase in appetite and weight gain noted in the first few weeks of treatment in the majority of the patients. It is believed that this drug may prove of lifesaving value in the severely debilitated, anorectic, malnourished subject who does not present any specific indication for steroid therapy. It is also suggested that the same calculated risk and precautions be taken for the use of dexamethasone as for the other steroids in the presence of gastrointestinal symptoms and diabetes mellitus. Although difficult to evaluate in a series of this moderate size, the minor side-effects did not seem to be much greater with dexamethasone than with the other steroids.

PUBLIC HEALTH

Some Factors Associated with the Development of Coronary Heart Disease: Six Years' Follow Up Experience in the Framingham Study. T. R. Dawber, W. B. Kannel, N. Revotskie and others. Am. J. Pub. Health 49:1349-1356 (Oct.) 1959 [Albany, N. Y.].

The National Heart Institute has been conducting at Framingham, Mass., a study of factors related to the development of cardiovascular diseases. A group of persons, consisting of two-thirds of the adult population and ranging in age from 29 to 62 years, was chosen at random for study. It was possible to bring in for examination 4,469 persons, 2,024 being men and 2,445 women. A group of 740 volunteers was added to supplement the initial group for prospective study. Follow-up of this group has been carried on for 4 biennial examinations, representing 6 years of observation. The data from this study show a significant trend in the incidence of coronary heart disease in relation to educational status, the incidence being lower at higher educational levels. There was no association between national origin of the persons and the risk of coronary heart disease. A suggestive low incidence of coronary heart disease was noted in one of the 8 Framingham precincts. This precinct differed from the others in some respects, but no explanation of this finding could be given.

Smoking was associated with an increased incidence of nonfatal myocardial infarction and of death from coronary heart disease in men between the ages of 45 and 62 years, and the risk was rising with the number of cigarettes smoked per day. But smoking was not associated with an increased incidence of angina pectoris. Cholesterol levels were higher among cigarette smokers than among nonsmokers, and they were higher among those who had smoked and stopped than among those who had never smoked. Neither the relative body weight nor blood pressure showed similar association with smoking. Alcohol consumption in itself did not show any relation to the development of coronary heart disease, although ingestion of large amounts of alcohol was associated with heavy smoking.

Pertussis Immunization in Pediatric Practice and in Public Health. R. W. Provenzano, L. H. Wetterlow and J. Ipsen. New England J. Med. 261:473-478 (Sept. 3) 1959 [Boston].

The purpose of this study, which was jointly undertaken by a pediatrician and 2 public health immunologists, was to compare the antibody response of 146 children to plain pertussis vaccine followed by triple [DPT] vaccine (diphtheria and tetanus toxoids combined with pertussis vaccine and aluminum phosphate precipitated) or to plain pertussis vaccine alone. The 146 children were divided into 4 groups: 66 children received 3 doses of DPT; 38 children received 3 doses of plain pertussis vaccine and 2 doses of DPT; 22 children received 3 doses of DPT and 1 booster dose of DPT; and 20 children received 3 doses of plain pertussis vaccine, 2 doses of DPT, and 1 booster dose of DPT. The 3 doses of plain pertussis vaccine were 0.5 ml., 1.00 ml., and 1.00 ml., and the doses of triple vaccine consisted of 0.5 ml. each.

The agglutination tests revealed that the average response in the group which received 3 doses of DPT alone was significantly lower than the responses in any of the other 3 groups. There was no significant difference between the mean response in the other 3 groups. The combined treatment of 3 plain pertussis doses and 2 DPT doses gave about twice as high a titer as 3 initial doses of DPT. A booster dose, given a year or more later, brought the titer up to the same level in all groups, and this level was not significantly higher than the one obtained after the initial series with 3 doses of plain and 2 doses of triple vaccine.

There was no evidence that children under 3 months of age were less responsive to pertussis immunization than older children. Noteworthy reactions, consisting of local swelling, soreness, and slight temperature, were observed in 19 children (7%) out of a total of 292 who were vaccinated. The authors do not recommend a change in the already established program of child immunization against pertussis. They further suggest that there should be no delay in the administration of booster injections.

BCG and Vole Bacillus Vaccines in the Prevention of Tuberculosis in Adolescents: Second Report to the Medical Research Council by Their Tuberculosis Vaccines Clinical Trials Committee. P. D'A. Hart, C. M. Brown, J. Charles and others. Brit. M. J. 2:379-396 (Sept. 12) 1959 [London].

The early results of a controlled clinical test of BCG vaccine and Mycobacterium tuberculosis var. muris (vole bacillus) vaccine in the prevention of tuberculosis in 56,700 boys and girls, who were between the ages of 14½ and 15 years and in their final year at secondary modern schools in or near North London, Birmingham, and Manchester, were published by the authors in a previous paper, an abstract of which appeared in The Journal (161:476 [June 2] 1956). The participants in this clinical test are now (1959) young men and women, aged between 21 and 23 years. In this second paper, the authors report results obtained after each participant had been in the clinical test for 5 years, with preliminary incomplete information up to 7½ years. Of the 56,700 participants, classified into 5 test groups while still in school, 13,300 with a negative reaction to 100 tuberculin units were left unvaccinated; 14,100 with a negative tuberculin reaction were vaccinated with BCG, and 6,700 with a negative tuberculin reaction were vaccinated with vole bacillus; 16,000 had a positive reaction to 3 tuberculin units, and 6,600 had a positive reaction to 100 tuberculin units but not to 3 tuberculin units. The participants in all 5 test groups were followed intensely by means of routine periodic roentgenographic examinations and tuberculin tests, individual contact also being maintained by postal inquiries and visits to the home. All definite and suspected cases of tuberculosis discovered by these methods or by information obtained from medical health officers or chest clinic records were reviewed for final diagnosis by an independent assessor, unaware both of the results of all the tuberculin tests and of whether vaccination had been performed.

Definite cases of tuberculosis beginning within 5 years of entry into the clinical test numbered 349. Pulmonary tuberculosis was present in 70% of these cases, and pleural effusion without evidence of pulmonary tuberculosis in 17%. Seventy per cent of the 349 cases were severe enough to require discontinuance of work for at least 3 months; cavitation was revealed by chest roentgenograms in 32% of those with pulmonary tuberculosis, and more than 2 rib interspaces were involved in 28%. There was one death from tuberculosis in the 5-year period. The annual incidence of tuberculosis in the BCG-vaccinated group was 0.38 per 1,000, compared with 2.29 per 1,000 in the tuberculin-negative unvaccinated group; this represents a reduction, attributable to vaccination, of 83%. Over the same period, the annual incidence of tuberculosis in the vole-bacillus-vaccinated group was 0.33 per 1,000, compared with 2.62 per 1,000 in the tuberculin-negative unvaccinated group; this represents a protection of 87%. The protective efficacy of each vaccine was thus substantial and was closely similar to that found for the first 2½ years in the earlier report. Supplementary incomplete information beyond 5 years showed that similar high levels of protection have continued up to at least 6½ years after entry into the clinical test. The degree of protection was similar for pulmonary tuberculosis, for tuberculous pleural effusion, and for enlargement of hilar lymph nodes associated with other lesions. Since 4 cases of tuberculous meningitis and 4 of miliary tuberculosis were observed among the tuberculin-negative unvaccinated participants, but none among those who were vaccinated, the degree of protection may have been greater for these forms. There was a suggestion also that the lesions in the vaccinated participants were less extensive and less severe than those in the unvaccinated participants.

Those entrants into the test whose positive reactions to 3 tuberculin units were strong (indurations of 15 mm. or more) had an annual incidence of tuberculosis of 3.50 per 1,000 in the first 2½ years, 1.76 in the second 2½ years, and 0.88 in the (incomplete) 5 to 7½ year period. In contrast, the annual incidences among those with weaker positive reactions to 3 tuberculin units and among those with positive reactions only to 100 tuberculin units were, respectively, 0.77 and 0.73 per 1,000 in the first 2½ years, and remained at much the same level thereafter. Thus, in this age group, there was a special risk of developing tuberculosis during the following years in those highly sensitive to tuberculin. Those with lesser sensitivity to tuberculin on entry into the test had consistently lower rates than those in the tuberculin-negative vaccinated group, suggesting that they had some degree of protection against fresh infection, though not as great as that in the vaccinated groups.

BOOK REVIEWS

The Surgeon and the Child. By Willis J. Potts, M.D., Surgeon in Chief, Children's Memorial Hospital, Chicago. Cloth. $7.50. Pp. 225, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5: 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

This is a lucid and easily readable description of an approach to pediatric surgical problems by one of America's best known surgeons. Consideration for the child as a person dominates the author's approach; from the sympathetic understanding made evident by his superb descriptions of sick children, it is not difficult to see why he is often referred to as an operating physician rather than simply as a surgeon. This book should appeal to both the pediatrician and the pediatric surgeon, as it contains many clinical clues and surgical points which should be helpful to both.

Some readers will regret the lack of a bibliography, but the absence of reference numbers strewn throughout the text makes for easier reading, and the scholar should have access to the Quarterly Cumulative Index Medicus. In a textbook of this size certain descriptions must occasionally be too brief, as is the description of the electrocardiogram of pulmonic stenosis. The prognosis of postoperative tricuspid atresia is a little too optimistic. One might question the choice of a pulmonary-artery pressure of 80 mm. Hg as the dividing line between patients with ventricular septal defect for whom the risk is good and those for whom it is poor; if anything should be emphasized, it is the severity of the pulmonary vascular resistance rather than the pressure. But these are minor points. Every page of this volume is written in a personal and conversational style and contains authoritative information that is essentially practical and simply presented. The book is well worth purchasing.

Pancreatitis: A Clinical-Pathologic Correlation. By Herman T. Blumenthal, Ph.D., M.D., Director, Institute of Experimental Pathology, Jewish Hospital, St. Louis, and J. G. Probstein, M.D., Associate Professor of Clinical Surgery, Washington University, School of Medicine, St. Louis, with foreword by R. M. Zollinger, M.D., Professor and Chairman, Department of Surgery, University Hospital, Columbus, Ohio. Cloth. $9.50. Pp. 379, with 58 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publication, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

A special interest in pancreatitis at the Jewish Hospital in St. Louis dates from 1934, when Dr. Somogyi developed a practical method for the determination of diastase in the blood. The subsequent 25 years of research form the background for the present volume. The subject is approached primarily from the standpoint of the pathologist, but the surprisingly high incidence (44 cases in 1,000 autopsies) suggests that pancreatitis has received insufficient attention in the past and that there is a real place for a book of this type. Comparatively few of these cases were judged to be clinically significant, but the occurrence of pancreatitis in association with nutritional, metabolic, endocrine, vascular, and other systemic diseases is of interest to clinicians. A large portion of the book consists of a critical review of more than 1,000 of the more significant contributions to the literature on pancreatitis, but interest is maintained throughout by the authors' stimulating commentary on the work of others in the light of the findings in their own series. In the chapter on pathological physiology, there is a particularly interesting discussion of some of the unanswered questions with regard to the pathogenesis of pancreatitis. What, for example, is the role of enzyme inhibitors in preventing pancreatic necrosis? Is the process initiated by collagenase which is secreted in its active form and not as a precursor?

Less than one third of the text is devoted to the clinical manifestations and treatment of pancreatitis, but the discussion develops smoothly and logically from the preceding sections on etiology and pathological anatomy and physiology and does much to elucidate some of the puzzling clinical features. The authors have achieved their purposes of focusing attention on pancreatitis and providing the means for evaluating the cause, pathogenesis diagnosis, and therapy, and of indicating problems for future study. They have also provided a comprehensive and up-to-date review of the voluminous literature on the subject.

Color Atlas and Management of Vascular Disease. By William T. Foley, M.D., F.A.C.P., Associate Professor of Clinical Medicine, Cornell University Medical College, New York, and Irving S. Wright, M.D., F.A.C.P., Professor of Clinical Medicine, Cornell University Medical College. Cloth. $18. Pp. 170, with illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1959.

The use of colored illustrations to describe typical forms of vascular disease is most logical, since changes in circulation manifest themselves in distinct patterns of pallor, cyanosis, rubor, mottling, ulceration, and gangrene. The authors for many years have been collecting colored slides which are commercially available, and the pictures presented in this atlas are no doubt reproductions from this collection. The cost of color printing is so great that it must have financial support from foundations, organizations, or private citizens. The authors have been fortunate in obtaining such help.

Naturally, the colored reproductions are not uniformly instructive. Pallor on elevation and rubor in dependency, which is a typical teaching demon-

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated

stration, is poorly represented. No illustration is given of a triphasic Raynaud's phenomenon, which would serve as an excellent example of visual education. Many of the illustrations would have been equally useful in black and white. In case 52 (scleroderma) the dark hair and yellow blouse of the patient is striking, but the typical pale yellow face with patches of pigmentation and the tight thin upper lip are not shown. Generally speaking, however, the color adds a great deal to the presentation of characteristic vascular patterns.

The text of the atlas is biased by the authors' experience with the medical therapy of vascular disease, coupled with an occasional grudging admission of surgical indications. This is unfortunate, since in the best interest of the patient there should be no medical or surgical viewpoint as such, but rather a well-balanced integrated judgment leading to proper selection of treatment for various conditions. It is interesting to note that in large group clinics internists have tended to become surgically minded, whereas surgeons often become more and more conservative. This book represents an extreme viewpoint of conservatism, and while frequent mention is made of futile or harmful surgical procedures, the unnecessary damage due to procrastination is ignored. If the general practitioner, to whom this atlas is addressed, is made to believe that an arterial embolus should not be extracted after eight hours or that a communicating feeder vein under a postphlebitic ulcer should be and can be injected with a sclerosing solution, then he will not serve the best interest of the patient.

On the other hand, the authors' valuable contributions to the treatment of claudication by walking exercises and the emphasis on the elastic support and postural treatment of lymphedema deserve wide acceptance. The angiocardiograms of pulmonary embolism are spectacular. The roentgenograms are hazy and most of them are so much reduced that detail can not be recognized. It is strange that the technical prowess shown in pharmaceutical advertisements or in the foreign illustrated news cannot yet be brought into use for medical communications.

All in all, read critically and with reservation, this volume contains much valuable material. The atlas is a worthy effort and should stimulate others to a less inclusive but more striking pictorial review of vascular disease.

A Synopsis of Obstetrics and Gynæcology. By Aleck W. Bourne, M.A., M.B., B.Ch. Twelfth edition. Cloth. $8. Pp. 632, with 167 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; John Wright & Sons, Ltd., 42-44, Triangle West, Bristol 8, England, 1959.

The 12th edition of this extraordinary book appears five years after the publication of the 11th edition, which required a second printing. This new edition should be received with similar enthusiasm. Although 100 pages of text have been added, the book remains compact, and its bulk has not been increased appreciably. The enlargement of the book is not due to the inclusion of new chapters but rather to the addition of new and supplementary information. The revised edition is astonishingly complete for so small a volume. New concepts have been included, new diagnostic and therapeutic procedures are described, and the descriptions of both gross and microscopic gynecological lesions have been extended. Outmoded concepts have been carefully deleted (excepting that relating to symphysiotomy, which is still presented in most British textbooks). Although the assembling of this enormous material into a small volume was accomplished by using the outline form and involved a sacrifice of literary style to brevity, the work is remarkably readable.

The book is intended principally for students, as a supplement to rather than a substitute for standard textbooks. It permits an orderly review of subjects already studied and should also clarify many subjects by providing succinct and general coverage, in a page or two, of matters to which standard textbooks may devote a chapter. In addition to its value to the medical student, the book should also be of great assistance to the teacher. It may be an excellent point of departure for the preparation of standard lectures and may also be of considerable help in the organization of occasional "spot" lectures which all teachers are called on, from time to time, to present on a moment's notice. The type is legible, the paper is of satisfactory quality, and the binding is adequate. The pen and ink drawings which illustrate portions of the text are appropriate and helpful. The book is enthusiastically recommended for medical students, teachers, and for practitioners who may wish to review this field.

Molecules and Mental Health. Edited by Frederic A. Gibbs, M.D., Professor of Neurology, University of Illinois College of Medicine, Chicago. Papers from scientific conferences of Brain Research Foundation: Amines in relation to brain function and behavior; ACTH treatment of hypsarhythmia. Published for Brain Research Foundation. Cloth. $4.75. Pp. 189, with 52 illustrations, J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6; Pitman Medical Publishing Company, Ltd., 39 Parker St., London, W. C. 2, England, 1959.

This book is the verbatim report of two symposiums held under the auspices of the Brain Research Foundation, and it deals with two subjects not closely related. The first symposium dealt with amines in relation to brain function and behavior and was held under the chairmanship of Drs. L. J. Meduna and Hudson Hoagland. Much that is controversial was discussed. There is a consideration of current work on ceruloplasmin in mental illness, but a question is raised about the method used in testing for this enzyme and consequently about the part that it may play in mental disease. The interesting work by Dr. R. G. Heath on the action of so-called taraxein in schizophrenia is also discussed, but no definite conclusions are drawn.

Somewhat less controversial are presentations of the use of hallucinogenic compounds in man, the excretion and metabolism of epinephrine and levarterenol in man, and the use of central nervous system stimulants.

The second symposium, under the chairmanship of Drs. W. L. Crawford and J. F. Bosma, dealt with ACTH treatment of hypsarhythmia. This also is controversial; the term hypsarhythmia refers to an electroencephalographic diagnosis applied to a childhood illness characterized by massive spasms, mental retardation, and gross electroencephalographic changes. As brought out by Drs. Peter Kellaway, C. M. Poser, and others, there may be multiple causes for this condition, so it is difficult to evaluate the response of a limited number of patients to steroid therapy. This book is interesting to one dealing with mental disease and epilepsy, but its format and presentation are likely to confuse the reader. Few of the essayists are adequately identified, and the various discussants, some of whose statements are much more important than those of the essayists, are identified only by their last names. Some of the presentations are extremely brief and center around motion picture demonstrations. Many of the discussions are irrelevant and deal with such matters as when the meeting should be recessed for lunch or who should make the closing statements. On the other hand, some of the material, such as Dr. Kellaway's discussion of hypsarhythmia, is excellently presented. On the whole, however, the book would be much more valuable to the reader if it were abridged and carefully edited and if only the necessary and revealing statements were included. The purpose and value of the book are diminished by the method of presentation here used.

Klinik und Therapie der Vergiftungen. Von Sven Moeschlin. Third edition. Cloth. 59 marks; $14.05. Pp. 655, with 92 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

This new edition of an excellent monograph deals with the clinical aspects of diagnosis and treatment of poisoning. Since the first edition, published in 1952, the incidence of poisoning has been increasing as new chemicals, for the most diversified purposes, have been placed on the market. The purpose of this book is to reorganize our knowledge of the clinically important poisons in a fashion which will most readily aid the general practitioner, internist, and medical student.

The work has retained the original format. The introductory chapter is followed by a carefully chosen bibliography, the classification and frequency statistics of poisonings presented in tables, general principles for the treatment, and revised maximum allowable concentration data on chemicals. The most important groups of poisonous chemicals are discussed in succeeding chapters. The emphasis throughout is on the chemicals that most frequently produce casualties. The chapters dealing with insecticides, lead compounds, acetophenetedin, and sleeping pills were completely revised. For each chemical there is a short synopsis of the signs and symptoms it may produce and the treatment required. A list of references is given at the end of each description.

The information needed by the clinician for the accurate detection and successful treatment of accidental poisonings is provided in the concluding chapter, along with a description of the pathological changes in different organs and functions produced by various chemicals. When confronted with a case of suspected poisoning the physician should turn first to this section where he will find, under the list of symptoms he has observed, a list of toxic substances which may cause them. The illustrations increase the practical value of the book. The index lists references, names of chemicals, and symptoms. This book can be recommended as an outstanding contribution of its kind. It is hoped that an English translation will be forthcoming soon.

Transactions of the 18th Conference on Chemotherapy of Tuberculosis, February 1959. Prepared and edited by VA Department of Medicine and Surgery, Central Office, Washington 25, D. C., and St. Louis area Medical Office. Held February 2 through 5, 1959, at St. Louis Medical Society Auditorium and Hotel Coronado, St. Louis, Missouri, by Veterans Administration—Armed Forces with cooperation of National Tuberculosis Association. Paper. Pp. 479. U. S. Veterans Administration, Department of Medicine and Surgery, Washington 25, D. C., 1959.

Even the editor of this volume states in the foreword that the preparation of a brief summary of the studies reported and their findings is a large order and he prefers "to walk around it." Thus one can only hope to sketch a few highlights and leave the future to decide which of these reports will prove of lasting value. Those included deal with the results of an original course of chemotherapeutic study, riboflavin, isoniazid (alone and combined with PAS), genetic factors, large high and small doses, toxicity, virulence, strpetomycin, re-treatment, treatment failures, pyrazinamide, cycloserine, the tuberculin test, tuberculosis in the very old, tuberculous meningitis, hydrocortisone, corticosteroids, prednisone, triiodothyronine, unusual acid-fast organisms, scotocleronogens, precipitation tests, DDS (diaminodiphenyl sulfone), B 111, pneumonectomies, coccidioidomycosis, amphotericin B, thiocarbonidin, streptovaricin, kanamycin, and committees' plans. General regimen studies showed differences in absolute results because of dissimilar design. Cycloserine toxicity may be controlled by sedatives, anticonvulsants, and tranquilizing agents; pyridoxine bioassays may be replaced by biochemical methods for serum and plasma levels of free isoniazid. Thiocarbanidin was effective and bacilli resistant to this drug were not observed. Patients treated with steroids and standard regimens showed roentgenographic evidence of improvement. In spite of the mass of data presented, evidence of progress can be detected. The summaries in the papers help to crystallize the points of the papers. The value of the discussion in some cases is questionable, and certainly much of it could have been omitted.

Fundamentals of Gynecology. By Samuel J. Behrman, M.B.Ch.B., M.S., M.R.C.O.G., Associate Professor, Obstetrics and Gynecology, University of Michigan Medical School, Ann Arbor, and John R. G. Gosling, M.D., Assistant Professor, Obstetrics and Gynecology, University of Michigan Medical School. Cloth. $9.50. Pp. 416, with 167 illustrations. Oxford University Press, 417 Fifth Ave., New York 16, 1959.

The authors have developed a concise, well-organized textbook of gynecology, primarily for their students but useful to any student or graduate student of gynecology. While the work is basically in outline form, it includes a wealth of essential material which will provide not only a good knowledge of the subject, but an understanding of it as well. Although concise, it still contains enough background or historical material to give depth to the study of gynecology. The book is adequately illustrated and is printed on good paper. It provides a chart giving a partial list of endocrine products used in gynecology, with the name of the manufacturer, rate of administration, and dosage.

The first part covers anatomic considerations, including evaluation of the gynecologic patient, anatomy of the female pelvis, uterine displacements, and urinary incontinence. The second part deals with menstruation, abnormal uterine bleeding, amenorrhea, dysmenorrhea, the menopause, virilism, and intersexuality. Part three covers leukorrhea, inflammation of the upper and lower genital tract, genital tuberculosis, and granulomas of the female genitalia. Part four takes up fibroids, endometriosis, and ovarian tumors. Part five deals with malignant tumors of the female genital tract. Part six covers abortion, ectopic pregnancy, hydatidiform mole, choriocarcinoma, infertility, and birth control. Part seven gives general principles and discusses lower abdominal and pelvic pain and the principles of radiation treatment of gynecologic neoplasms. Most of the references listed are recent. The book is written in easily understandable style.

A Text on Systemic Pathology. Volume II. Edited by Otto Saphir, M.D., Director, Department of Pathology, Michael Reese Hospital, Chicago. Cloth. $38. Pp. 867-1950, with illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1959.

All those responsible for diagnosis and requiring up-to-date information regarding disease should be pleased to know that the second volume of this authoritative work is now available. The chapters on the gastrointestinal tract, liver, and pancreas, written by the editor, maintain the high standard of the first volume. Max Appel has covered well the subject of endocrine glands, but these chapters are not as well illustrated as other portions of the book. This applies particularly to the pituitary. The sections on the oral cavity and the ear, by Szanto and Saphir, and on the eye, by Zimmerman, are far superior to those generally found in standard reference works of this size. The section on the skin is well written but inadequately illustrated. There is an excellent chapter on endocrine and vitamin disturbances of the bone by Amromin, who covers other diseases of the bones and joints equally well. The muscular dystrophies are not described as well as should be expected for work of this character, nor are the neoplasms. The central nervous system is ably discussed by Chason. In general, the photographs of gross specimens throughout the volume are superior to the photomicrographs. The bibliography is unusually complete and up to date. This type of reference work is highly valuable to those who need ready access to detailed information on pathological findings in disease.

Nutritional Diagnosis. By Grace A. Goldsmith, M.D., M.S., F.A.C.P., Professor of Medicine and Director, Nutrition-Metabolism Unit, Department of Medicine, Tulane University School of Medicine, New Orleans. Publication number 356, American Lecture Series, monograph in *American Lectures in Metabolism.* Edited by S. O. Waife, M.D., and Paul György, M.D., Professor of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia. Cloth. $5.50. Pp. 164. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The author is an experienced and respected physician and investigator in the field of human nutrition. She has prepared this review of current knowledge to assist the physician in evaluating and managing the nutritional problems of his patients. The book is timely in that it presents in succinct, authoritative form a resumé of all the important advances of recent years that have helped to improve the diagnosis of nutritional abnormalities. The usefulness of this kind of information is indicated by the many diseases which may be accompanied by nutritional disturbance. These are discussed in relation to each of the nutrients required by man. The author assesses the daily requirement of each essential nutrient. Manifestations of deficiency or excess are discussed. The limitations of presumptive diagnosis of specific deficiencies based on physical manifestations alone are stressed, and the assistance to be obtained from laboratory tests is evaluated. A carefully selected bibliography is included. The book is well written, easily read, and relatively free of publisher's errors. It should prove valuable to the large group of physicians who are confronted almost daily with nutritional problems. It should be pointed out, however, that the book is not exhaustive in its treatment of the subject, nor is it intended for the investigator who might require more complete discussion and reference material.

The Annual Survey of Psychoanalysis: A Comprehensive Survey of Current Psychoanalytic Theory and Practice. Volume V: 1954. Edited by John Frosch, M.D., and Nathaniel Ross, M.D. Lottie M. Newman, editorial assistant. Cloth. $12. Pp. 608. International Universities Press, Inc., 227 W. 13th St., New York 11, 1959.

This annual survey of the field of psychoanalysis has proved its worth over a period of several years. It is, as stated in the subtitle, a comprehensive survey of current theory and practice. The book might be of even greater value if it were published without the present five-year lag. The volume under review covers the literature for 1954. There are 10 subsections, including an excellent one on critiques by Dr. Leo Rangell. This section deals objectively with various critiques of psychoanalytic theory and practice and is a healthy indication of the acceptance of critical evaluations of psychoanalysis. This volume, because of its technical nature, will be of interest primarily to practicing psychiatrists and psychoanalysts. Some of the sections, however, may be read with profit by nonpsychiatrists. Chapter 10 contains summaries of 10 important books. These seem to have been selected both for their significance and as a spectrum of current problems in psychoanalysis. The bibliography and index are fine.

The Treatment and Prevention of Reading Problems (The Neuro-Psychological Approach). By Carl H. Delacato, Ed.D., Head of junior and middle schools, Chestnut Hill Academy, Philadelphia. Cloth. $4.50. Pp. 122, with 13 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The author introduces his subject by listing characteristics which were found to be not common, fairly common, and universal in a group of 45 boys who had reading problems. The data indicated that some neurological involvement was frequently an underlying cause. After searching neurological literature for answers to reading problems the author states that he was confused by the conflicting findings. He then developed a process by which persons might achieve a better neurological organization that would prevent reading problems or facilitate learning to read.

The rationale for the proposed tests for neurological disorganization and the methods for establishing neurological organization is not entirely clear. Procedures such as reducing fluid intake, controlling postures during sleep, establishing central dominance, and not listening to music are suggested, but no controlled experimental data are given. A reader with some knowledge of this subject is likely to find it difficult to accept all of the statements made. It is possible that some disorganization in the central nervous system can explain many reading problems. There would be much interest in a scholarly rationale for this hypothesis and more careful research to test its validity. The present book unfortunately does little to advance knowledge in this area.

Principles of Biochemistry. By Abraham White, Ph.D., Professor of Biochemistry, Albert Einstein College of Medicine, Yeshiva University, New York, Philip Handler, Ph.D., Professor of Biochemistry and Nutrition, Duke University School of Medicine, Durham, N. C., Emil L. Smith, Ph.D., Professor of Biological Chemistry and Research, Professor of Medicine, University of Utah College of Medicine, Salt Lake City, and DeWitt Stetten, Jr., M.D., Ph.D., Associate Director in Charge of Research, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md. Second edition. Cloth. $15. Pp. 1149, with illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farrington St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1959.

This second edition appears only five years after the first edition, but in the field of biochemistry certain areas are developing so rapidly that frequent revision is necessary. All sections of the book have been brought up to date, and some, such as those covering endocrinology and the metabolism of carbohydrates, lipids, proteins, and nucleic acids, have had to be either extensively revised or completely rewritten. This work is intended as a textbook for medical students in biochemistry and is exceptionally well organized and well written. The book is divided into seven sections which deal with the chemical composition of cells, catalysis, metabolism, body fluids, biochemistry of specialized tissues, biochemistry of endocrine glands, and nutrition. At the end of each chapter or at the end of a series of chapters on a single subject there are lists of references. The book is well indexed.

The Historical Development of Physiological Thought: A Symposium Held at the State University of New York, Downstate Medical Center. Edited by Chandler McC. Brooks and Paul F. Cranefield. Cloth. $6. Pp. 401, with illustrations. Hafner Publishing Company, Inc., 31 E. Tenth St., New York 3, 1959.

This report of a series of symposiums held in 1956 and 1957 to mark the centennial year of the founding of the medical school of the State University of New York, and to dedicate the Basic Science building of this school, presents essays that trace the development of current concepts of basic medical science from their earliest beginnings. Each author has approached this development from a different point of view, and the historical contributions to current physiological thinking that have arisen from general biology, anatomy, endocrinology, neurology, and other diciplines are traced in detail. The essays are scholarly and thorough and they cover much more than the development of physiological concepts; they spread over into such specialties of medicine as neurology and psychiatry. The book offers the reader a mass of historical information which is not readily available to most students. The bibliographies are extensive. The authors, renowned in their fields, include Temkin, Eccles, Fulton, Magoun, Rosen, and Gilman, to mention only a few. The volume should be of interest to all students of medicine and particularly to medical researchers.

Film Reference Guide for Medicine and Allied Sciences. By Interdepartmental Committee on Medical Training Aids (ICMTA). U. S. Department of Health, Education, and Welfare, Public Health Service, National Library of Medicine, Washington. Paper. $1. Pp. 192. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1959.

This guide has been reedited and issued yearly since 1957 and contains listings of medical films and filmstrips that are recommended for use in the medical programs of at least one of the member agencies of the Interdepartmental Committee on Medical Training Aids. The committee comprises representatives from each of the following federal government agencies: (1) Department of the Air Force, Office of the Surgeon General; (2) Department of the Army, Office of the Surgeon General; (3) Department of the Navy, Bureau of Medicine and Surgery; (4) Armed Forces Institute of Pathology; (5) Department of Health, Education, and Welfare, Public Health Service; and (6) Veterans Administration, Department of Medicine and Surgery. While this is, no doubt, an accurate catalog of films and filmstrips, it must be remembered that these are selected for use in governmental programs; the guide does not purport to be a complete list of available films.

Examination of Whole Cigarette Smoke by Light and Electron Microscopy. By Wanda K. Farr and Althea Revere. Paper. Pp. 109, with illustrations. Published as public service by Life Extension Foundation, 11 E. 44th St., New York 17, 1958.

This report gives the results of a study on cigarette smoke with use of both the light microscope and the electron microscope. The study includes 10 popular brands of cigarettes and is reported largely by photographic means with accompanying brief explanations.

Lexicon ophthalmologicum. Editores: M. E. Alvaro et al. [In English, German, Spanish, French, Italian and Latin.] Originally published in Switzerland by S. Karger, Basel. Cloth. $9. Pp. 217. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Avenue., Montreal 6, Canada, 1959.

This dictionary was prepared under the sponsorship of the International Council of Ophthalmology. The publication is a compilation of 2,192 terms, with equivalents in English, German, Spanish, French, Italian, and Latin. Complete information appears in the English language section, where terms are numbered in order. These numbers are then used for reference in the sections dealing with other languages. Actually, the figure quoted above is misleading because a number of entries are repeated in reverse order, e. g., under "loop, vascular" as well as "vascular loop." In some instances, the translations under the two entries do not agree. The dictionary should fulfill its purpose of helping the ophthalmologist to read, and perhaps write, in a language other than his own, and should be useful also to anyone studying, translating or abstracting the literature of this specialty.

The Physiology of the Newborn Infant. By Clement A. Smith, M.D., Associate Professor of Pediatrics, Boston Lying-in Hospital, Harvard Medical School, Boston. Third edition. Cloth. $12.50. Pp. 497, with 62 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The third edition of this work should serve as an excellent reference book for both the pediatrician and the general practitioner because it clearly indicates some of the physiological differences in the neonate as compared to the healthy growing baby. The mechanism of maintenance of body temperature, establishment of digestion, regulation of water balance, general metabolism, normal behavior, reflexes, circulatory system, blood, and liver function are discussed at length. There is a clinical summary at the end of each chapter and an extensive bibliography at the end of the book. The print and the type of paper are of high quality. This book would be a valuable addition to any medical library.

Principles of Pathology. By Howard C. Hopps, M.D., Professor and Chairman, Department of Pathology, University of Texas–Medical Branch, Galveston. Cloth. $6.95. Pp. 301, with illustrations by Lenore Megnin Sloan and George Newman. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1959.

This is a relatively simple and lucid description of the main pathological conditions. It is one of several American textbooks presenting the subject in an elementary manner readily comprehended by medical students. The mode of presentation differs from that of such authors as Paling Wright and Sir Howard Florey, who cover the same subject matter in a more detailed and scientific manner. The book contains no photomicrographs and no bibliographic substantiations of the numerous facts and generalizations presented. Whether such a book is considered adequate for medical students de- er or not in his opinion medical students are to be pends on the philosophy of the teacher and wheth- considered as potential clinical observers or as future run-of-the-mill practitioners of medicine.

Medicinal Chemistry. Volume IV: A Series of Reviews Prepared under the Auspices of the Division of Medicinal Chemistry of the American Chemical Society. By Wilbur J. Doran. Editors: F. F. Blicke and R. H. Cox. Associate editor: L. A. Woods. Asisstant editor: Harriet Greer. Cloth. $12. Pp. 334. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, England, 1959.

This volume contains a review of barbiturates. The subject is treated briefly from the chemical and pharmacological aspects. Most of the material is contained in tables, with references to the compounds. Other tables list generic and trade names as well as firms manufacturing barbiturates of therapeutic value. The book has both empirical formula and subject indexes.

QUESTIONS AND ANSWERS

POSTOPERATIVE CARE OF PILONIDAL CYST

To the Editor:—*What postoperative management is best after excision of a pilonidal cyst if primary closure of the wound has not been done? How does one keep granulation tissue from forming?*

Thomas W. Kredel, M.D., Indiana, Pa.

Answer.—In the early postoperative period the wound is clean and dressings need be changed only after four days. For the next two to three weeks the patient should be instructed to take sitz baths twice daily, wash the area with a germicidal soap, and apply a topical antibiotic. A small piece of gauze is used for separating the edges of the wound, to allow healing of the saucerized wound from the bottom up. All pockets that form are opened by the surgeon when he sees the patient at intervals of one to two days.

The third stage of postoperative care may linger for months if excessive granulation tissue forms. By this time, hair has grown back, with some hairs breaking off and gathering in the wound while others protrude into the granulation tissue, thus forming a chronic infection which may pocket off and make the surgeon believe that there is a recurrence of the pilonidal cyst. This, I believe, is the main reason for the excessive granulation tissue. The hair in the gluteal cleft should be shaved at intervals of 7 to 10 days, and treatment with sitz baths, soaping, and a topical antibiotic continued. The excessive granulation tissue should be removed periodically and not cauterized with silver nitrate.

Answer.—The best type of open operation for pilonidal disease is the marsupialization operation, because in this procedure the deep wall of the cyst is left in place and the wound edges are beveled and sutured down to it. This minimizes formation of granulation tissue.

Granulation tissue is minimized if the buttocks are held apart and the wound cleansed with hydrogen peroxide twice a day. Exposure of the wound to a 100-watt bulb, placed about 12 in. above the buttocks for one hour, will minimize maceration and promote healing. It should be close enough to give a mild degree of warmth without burning the patient. If granulation tissue forms, it should be cut away. Frequently, the appearance of an excessive amount of granulation tissue indicates that a small amount of cyst wall or sinus tract has remained; this will have to be removed before healing can result.

REACTION DUE TO TYPHOID IMMUNIZATION

To the Editor:—*What different reactions can occur in a patient after administration of an immunizing injection for typhoid fever? A 4-year-old child was given an injection in the left arm and the next day had pain and stiffness of the arm and fever, which is not unusual. On the second day his fever was higher and the arm had become swollen, red, fluctuant, and extremely painful down to the elbow. Rheumatic fever was one of the differential diagnoses, but the circumstances are so coincidental that one is tempted to credit the reaction to the typhoid immunization injection.*

Ruth C. Hagstrom, M.D., Starksville, Miss.

Answer.—The occurrence of rheumatic fever in a patient after typhoid vaccination has not been reported, but that of one instance of acute benign carditis has. Aside from the general systemic signs and symptoms of fever, malaise, and myalgia which may occur in about 25% of persons vaccinated, several other organ systems have been involved in post-typhoid-vaccination reactions, such as (1) nervous system reactions, such as acute ascending myelitis, an acute fatal case of multiple sclerosis, neuritis, polyneuritis, and bilateral median nerve paralysis; (2) cardiovascular reactions, such as cutaneous hemorrhagic reactions presumably on an allergic basis; bone marrow myeloblastic reactions, pancytopenia, and death due to myeloid insufficiency (19 days after vaccination); and (3) pulmonary complications, such as transitory pulmonary infiltrates and the finding of tubercles in the sputum of patients with arrested tuberculosis.

Other complications reported to occur after vaccination include postvaccinal nephritis with permanent renal damage, thought to be an allergic reaction; prolonged fever; death; and transient postvaccinal diabetes with coma, an anaphylactoid reaction.

On the basis of these syndromes after vaccination with typhoid vaccine, the diagnosis of rheumatic fever probably is correct. In this patient the injection may have influenced the precipitation of the clinical manifestations of rheumatic fever.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

VENOUS STARS

To the Editor:—*What is the cause and significance of "spider" veins, so often found in the thigh skin of women, with and without the presence of varicose veins? They seem to occur more frequently in young pregnant women and in women of menopausal age. What would be treatment for cosmetic effect?* M.D., *Michigan.*

Answer.—Venous stars or "spider" hemangiomas are related to increased venous pressure, except in the gravid woman in whom their development may be favored by hormones since they can appear before there has been any increase of venous pressure. They occur in men also and may be numerous in the patient with obstruction to the superior vena cava, when collateral circulation is being established. Most physicians do not recommend treatment, since most therapeutic efforts have been useless and some harmful.

These venous stars and other similar lesions are discussed in detail in Bean's "Vascular Spiders and Related Lesions of the Skin" (Springfield, Ill., Charles C Thomas, Publisher, 1958).

RASH ON CHEEKS AND EYEBROWS

To the Editor:—*A man who is a teacher has had a butterfly pattern appear on his cheeks and up into his eyebrows for 10 or more years. It is most apt to be evident after his exposure to tobacco smoke or when he is in contact with house paint or photographic chemicals. The area becomes red and slightly painful. It disappears after a few hours or days and may not recur for several weeks or months. Sometimes epidermal scales may be formed in that area, and below the red area of the left cheek there is a tiny papulovesicular lesion which has been there many years. What treatment would give this man permanent relief?* M.D., *Tennessee.*

Answer.—The description of the eruption as a "butterfly rash" on the face suggests the diagnosis of lupus erythematosus, but appearance of the latter usually is slow. Scaling takes place, and there are enlarged follicles, telangiectases, and in time atrophy. The lesions of the acute form of lupus erythematosus are not as fixed and may not have a perceptible degree of atrophy, and the patient has systemic symptoms, such as fever, joint pains, and other manifestations. The transient character of the skin changes are more likely to be due to a simple erythema, and, because of the scaling, a mild dermatitis is possible. The evanescent character of the eruption suggests a form of urticaria, or angioneurotic edema, which can be slightly painful, as was described by this patient, who may be allergic to a common substance in smoke, paint, and photographic chemicals. Attempts at isolation of the allergenic material and desensitization therapy are apt to be unsuccessful; hence, if the patient cannot avoid the irritants, antihistamine therapy may give relief or may be used prophylactically. Burow's solution, diluted 1 to 10 with water, can be used for wet dressings. Injections of ACTH or use of a steroid drug should give relief, but neither should be used without due consideration.

COPPER STAINING OF HANDS

To the Editor:—*A plumber who handles copper tubing in his work can wash the stain off his hands and forearms at the end of the day, but during the next one to two hours the perspiration formed in the axillas is copper-tinted. What studies might be done to rule out copper poisoning?* *Richard E. Passenger, M.D., Newburgh, N. Y.*

Answer.—The sweat from the axillary region should be collected and tested for the presence of copper by spectroscopic examination. It is not likely that it will show the presence of copper. There is a condition known as chromhidrosis which produces perspiration of various colors. These fluids, when placed under Wood's light, are fluorescent. There is a copper-colored fungus, Nocardia tenuis, which can flourish on the skin of the axillary region and cause yellow sweat.

Discoloration of the skin often takes place in persons handling copper, but this does not indicate actual injury from the copper. Should copper poisoning be demonstrated, the patient should change occupations.

TEST FOR UNTOWARD REACTION TO SUCCINYLCHOLINE

To the Editor:—*We use succinylcholine chloride in the treatment of our neuropsychiatric patients, and, prior to administration of the full dose, the patient is given a small amount so that we can see what his response will be. If there is a test which will predict the response of a patient to succinylcholine we would appreciate a summary of the test.* M.D., *Wisconsin.*

Answer.—A test to determine the probable amount of succinylcholine required to produce the optimal relaxation in a patient was published by David J. Impastato, M.D.

At the time of the first treatment, prior to the administration of the full therapeutic dose of succinylcholine dichloride, a test dose of 5 mg. of succinylcholine and 1 cc. of a barbiturate solution, containing 50 mg. of thiopental sodium or 25 mg. of thiamylal sodium, is mixed in a hypodermic syringe for intravenous administration. The strength of the patient's hand grip is ascertained by having him squeeze the physician's hand. The test dose is then given as quickly as possible, and the patient is asked to squeeze the physician's hand as firmly as he can. In this manner, the degree of the patient's muscular weakness is measured and the therapeutic dose of succinylcholine determined. The strength of the patient's hand grip should be tested intermittently, for one minute. The details of Dr. Impastato's procedure are given in his original article (*Am. J. Psychiat.* 112:893 [May] 1956), but he has since modified his procedure somewhat. A description of his modified test method is as follows:

The patient is given 1/50 of a grain (1.2 mg.) of atropine intramuscularly, one-half hour prior to treatment. No barbiturates are used. Just before treatment the patient is given 10 mg. or less of succinylcholine intravenously. Ten seconds later a petit mal electroshock stimulation is given, followed 20 seconds later with the usual grand mal electroshock stimulation. The patient is then managed in the usual manner.

It is not likely that the administration of fractional doses of succinylcholine can give more than a rough estimate of how a patient may react when he is given larger doses.

Editor's Note: Serious reactions to succinylcholine can occur, as reported by Kepes and Haimovici in The Journal, Oct. 3, page 548.

HYDROCELE

To the Editor:—*What is the cause and treatment of a hydrocele of the tunica vaginalis, which has been evident in a 7-year-old child for four weeks?*

William S. Levy, M.D., Woonsocket, R. I.

Answer.—The cause of a hydrocele occurring in a 7-year-old child is difficult to determine, and, in many instances, it will disappear spontaneously. Surgical management is usually not indicated in children of this age group, and I believe this could safely wait until adolescence for any definite therapy, unless the lesion becomes a mechanical problem or there should be any psychic disturbance in the patient.

SYMPTOMS OF PARADOXICAL EMBOLISM

To the Editor:—*Can paradoxical embolus simulate the clinical picture of dissecting aneurysm (peripheral paralysis and weakness in legs)? How can these two conditions be differentiated, if the patient has congenital heart disease with systolic or diastolic murmurs, or both, cardiac enlargement, and hypertension?*

Heino Trees, M.D., Washington, D. C.

Answer.—A large embolus, which stops at the aortic bifurcation (saddle embolus), might simulate dissection of the abdominal aorta by causing symptoms of abdominal pain, weakness in the legs, and signs of decreased pulsation in the circulation of the lower extremities. It would not simulate dissection of the thoracic aorta, in which the pain has a higher localization early in the process and later spreads downward. There are also changes in the brachial and carotid pulsations before any decrease in those of the femoral arteries. Smaller multiple emboli might block the femoral or tibial arteries, although it is not likely that the obstruction would be completely symmetrical.

Minute emboli to the spinal cord might cause paraplegia or perhaps a slight decrease of the tibial pulse through vasomotor disturbances. They would not cause abdominal pain (radiating downward) nor would they cause the disappearance of arterial pulsation in the lower extremities.

Paradoxical embolism occurs through an atrial septal defect only if there is right ventricular failure (possibly secondary to pulmonary embolism) or during unusual exertion (increase of venous return). It does not occur in uncomplicated ventricular septal defect or patent ductus. It can occur without any favoring cause if there is an overriding aorta (Fallot, Eisenmenger) and if the pressures of the two ventricles are equivalent.

Dissection of the aorta should be considered whenever the patient has weakening of the wall of the thoracic aorta (coarctation of the aorta with poststenotic dilatation; septic aortitis in patients with bacterial endocarditis). Hypertension, if severe, can be a factor causing dissection, but the most important cause of dissection is a degenerative lesion of the media, particularly a medionecrosis cystica.

PIGMENTED SPOTS IN ORAL TISSUE

To the Editor:—*A 43-year-old man has brown-colored areas on the lower lip, the upper gingival tissue, and the hard palate. The lesions vary in size and shape and are not elevated or tender. The lesion appeared on the upper gum about 15 years ago, after the patient had had dental repairs done and been given procaine in this area. What diagnostic tests would be indicated, and should biopsy be included? The rest of the physical examination was normal.*

Owen L. Murphy, M.D., Simsbury, Conn.

Answer.—It is impossible that these lesions could be a local pigmentary reaction to procaine for the pigmentation has occurred in areas distant from both the normal site of injection and the areas to which the procaine normally would diffuse.

Biopsy might determine both the type of pigment present and its location. If available, spectroscopic analysis of biopsy material could identify the pigment.

A condition suggested by the description is Peutz-Jeghers syndrome (hereditary multiple polyposis). This syndrome is rarely encountered and usually familial. Pigmentation occurs in the buccal mucosa and sometimes on the palms and fingers. It is accompanied by multiple, widely scattered intestinal polyps, which may or may not be a cause of diarrhea, and by intestinal bleeding. A complete investigation, with this condition in mind, could establish the diagnosis. There is no treatment for the pigmentation.

WASHINGTON NEWS

Federal Health Spending Rises . .

Eisenhower Position on Aging . .

Influenza Investigations . .

Committee Shifts . .

FEDERAL MEDICAL-HEALTH BUDGET CLIMBS

Spending on the federal government's medical and health activities in the fiscal year starting July 1 will reach the highest levels in history, under the budget proposed to Congress by the Eisenhower administration.

The Department of Health, Education, and Welfare, parent agency of the Food and Drug Administration, the Public Health Service, and the Social Security Administration, among others, is scheduled to spend 3.5 billion dollars next year, 100 million dollars more than during the current fiscal year.

Actually, if welfare and education programs are taken into account, along with social security outlays (not included in the budget) and public assistance grants, spending in the medical-welfare-education field would total about 15 billion dollars. This would rank second only to defense as a spending item of the federal government. Of course, the Veterans Administration and armed services operate extensive medical programs of their own.

President Eisenhower sought an appropriation of 400 million dollars for the National Institutes of Health, the chief medical research agency of the government. This was the sum voted by Congress last year when the lawmakers approved 106 million dollars more than the budget request.

In this budget message to Congress, the Chief Executive said, "Advances in medical technology and the spread of private insurance have played important roles in raising the level of health services for our rapidly expanding population." He added, however, "The growing demand for better health care has contributed to shortages of facilities, medical and scientific manpower, and supporting health workers, as well as to the rising cost of medical and hospital services."

"In order to deal effectively with these developments, the federal government has expanded its public health programs and is actively seeking solutions to the nation's health problems," said Mr. Eisenhower.

The President warned against waste, asserting that the HEW Department "will insist on maintaining high standards in determining the acceptability of medical research projects for federal support."

"It is essential that federal grants for these projects be so administered that medical manpower is not unduly diverted from other pressing needs and that federal funds are not substituted for funds from private sources," said Mr. Eisenhower.

The medical-health budget contained one new legislative proposal—to establish a $4,700,000 program "to support research and informational projects in foreign countries which hold promise of contributing significant knowledge in the fields of health, education, and welfare." About $3,700,000 of this would be for medical research. This plan, if approved by Congress, would have little effect on government spending, since the funds would come from the government's program of shipping surplus farm goods abroad in return for foreign currency payments to be used in the countries involved as a form of foreign aid.

Another significant development was the setting up of a combined, expanded Public Health Service program for combating air and water pollution and radiation dangers. The budget asked $23,400,000 for these activities, $6,100,000 more than last year. Most of the increase was for more checking of radiation levels to determine if they pose a national health problem.

HILL-BURTON

As President Eisenhower had forecast earlier, only one HEW program was slated for a money cut—the Hill-Burton plan of assisting states and localities to build and expand hospitals. The appropriations request of 125 million dollars for Hill-Burton was 60 million dollars less than last year's sum. Because of a carry-over of funds from this year that have already been allocated, however, the hospital program will cost $159,800,000 next fiscal year, up from the $142,800,000 this year.

In the budget message, Mr. Eisenhower said the recommended hospital appropriations "will assure that sufficient new general hospitals can be financed to keep pace with the population growth, cover current obsolescence rates, and provide for 6,000 new beds to reduce the backlog of needs."

FOOD AND DRUG ADMINISTRATION

The Food and Drug Administration staff would be increased almost 19% under the administration's budget. The extra money would increase the number of field inspectors from 499 to 593 men. The money recommendation totaled $18,200,000, $2,700,000 over this year's level. The additional sum will enable the agency "to provide greater protection for the consumer against harmful, unclean, and misrepresented foods, drugs, and cosmetics," said HEW Secretary Flemming.

VETERANS ADMINISTRATION

Services and benefits spending by the Veterans Administration was scheduled to be increased to 5.5 billion dollars from the 5.2 billion dollars this year. Of this total, 928 million dollars would go for hospital and medical care, a jump of 22 million dollars.

MEDICARE

As the result of a liberalization that went into effect the first of the year, costs were expected to increase for the Defense Department's program of treating qualified dependents of military personnel in civilian hospitals. Spending for the next fiscal year was placed at $70,300,000, compared with $68,500,000 this year. Congress appropriated $88,800,000 for the program last year.

VOCATIONAL REHABILITATION

Funds for the program of aiding the handicapped to rehabilitate themselves in jobs was boosted to $71,200,000, an increase of 5 million dollars. Of the total, $54,500,000 will be for grants to states and localities for their rehabilitation programs.

NIH BREAKDOWN

All nine divisions of the National Institutes of Health were scheduled to spend more next fiscal year. The breakdown comparing spending in this fiscal year and next is as follows: Division of General Medical Sciences, 45 million dollars and $47,500,000; Cancer, $73,700,000 and 81 million dollars, Mental Health, $65,400,000 and $68,500,000; Heart, $57,900,000 and 62 million dollars; Dental, $9,500,000 and 11 million dollars; Arthritis, $42,300,000 and 46 million dollars; Allergy, 33 and 35 million dollars; and Neurology and Blindness, 37 and 39 million dollars.

HEALTH SURVEY

A new health examination survey was proposed to supplement the present household interview survey conducted by PHS. Under the program, mobile units will be used to conduct physical and clinical examinations of representative samples of the population. To finance the plan, the administration asked $2,100,000, 46% above the $1,500,000 requested last year.

INDIRECT RESEARCH COSTS

The administration again urged removal of the existing 15% limitation on indirect costs for grants for medical research. This has repeatedly been recommended by the American Medical Association, universities, and consultants who have pointed out that the limitation places an unfair burden on schools and institutions which often must bear more than 15% of the cost of a federally financed research project.

PRESIDENT CALLS FOR COOPERATIVE EFFORT ON AGING PROBLEMS

President Eisenhower indicated that he believes any major efforts to solve problems of the needy aged in this country should be held off until after the White House Conference on Aging next January.

In his budget message to Congress, he said the conference and the state conferences which precede it "should help point the way toward more productive and satisfying living for our aged citizens."

"The health, employment, income, and other needs of the increasing number of elderly people in our population can be met only through the combined efforts and cooperation of private, local, state, and federal organizations and agencies," the President declared.

"Advances in medical technology and the spread of private insurance have played important roles in raising the level of health services for our rapidly expanding population," continued Mr. Eisenhower. In a later message to Congress—the President's annual economic report—Mr. Eisenhower said, "health services are more and more widely available, and the great majority of Americans now have some protection under voluntary plans of hospital, surgical, and medical insurance."

Although he did not mention it by name, the President implied opposition to the Forand bill that would provide compulsory financing of partial health care for the elderly through the social security system.

STUDIES ON INFLUENZA

The Public Health Service announced it will expand its influenza research program "to take advantage of the study opportunities afforded by the current influenza outbreaks."

All research projects in the field were scheduled to receive special review at the National Institutes of Health, and qualified projects will be approved rapidly, according to the service. Members of the PHS Committee of Investigators agreed at a meeting called here to accelerate their own research during the influenza season and to encourage other investigators to conduct studies on influenza.

Types of problems deserving priority research, the committee said, were (1) assessment of the value of vaccine given in the 1957 epidemic as to its possible degree of protection this year; (2) the present degree of immunity of unvaccinated persons who had influenza in the 1957 epidemic; (3) the physiological effects of influenza on cardiovascular and respiratory systems; and (4) the neuromuscular effects of influenza.

KEY COMMITTEE POST CHANGES

Some important vacancies on congressional committees that handle legislation of interest to physicians were filled in the early days of the session.

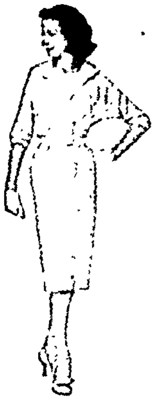
Sen. Thruston B. Morton (R., Ky.), who is also GOP National Chairman, replaced Sen. Norris Cotton (R., N. H.) on the influential Senate Finance Committee that handles tax legislation. Senator Morton is a sponsor of the Keogh-Simpson measure to provide tax deferrals on money set aside by self-employed persons for their retirement. Senator Cotton was transferred to the Senate Judiciary Committee.

Rep. John A. Lafore (R., Pa.) was placed on the House Ways and Means Committee to fill the vacancy left by the late Rep. Richard M. Simpson (R., Pa.), who had been ranking Republican member of the committee. Representative Lafore, like his predecessor, is a strong foe of the Forand proposal to extend the social security system to include partial financing of health care for elderly beneficiaries.

...threatened abortion

...habitual abortion

...endometriosis



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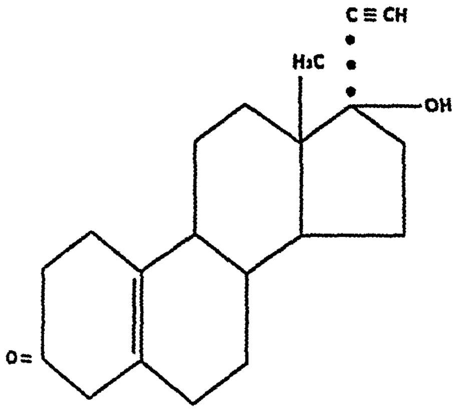

NORETHYNODREL, the principal constituent of Enovid, is the only progestin with the double bond in the position shown, thus differing from androgens and estrogens. Norethynodrel possesses intrinsic estrogenicity (3 to 7 per cent that of estrone) in addition to its potent progestational activity.

Thus, its administration is free of risks of virilism even on long-term administration at high dosage.

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2. Retains its biologic integrity[2] following oral administration.
3. Is progestational and estrogenic in experimental animals.
4. Is progestational and estrogenic in clinical practice.
5. Is not androgenic[1] in experimental animals.
6. Is not androgenic[3] in clinical practice.

Enovid represents a positive advance in the treatment of threatened or habitual abortion[4] and in the treatment and control of endometriosis[5]. Physicians may prescribe Enovid confidently without producing androgenic manifestations.

DOSAGE OF ENOVID FOR THREATENED ABORTION

Two or three tablets daily on appearance of symptoms. This dosage may be reduced to one or two tablets daily when symptoms disappear. The reduced dosage should be continued to term and increased if symptoms reappear.

DOSAGE OF ENOVID IN HABITUAL ABORTION

Two tablets daily as soon as pregnancy is diagnosed and continued without interruption at least through the fifth month. Enovid may be safely continued to term if desired.

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1. Symposium on New Steroid Compounds with Progestational Activity, Ann. New York Acad. Sc. 71:483-805 (July 30) 1958.
2. Edgren, R. A.: The Uterine Growth-Stimulating Activities of 17α-Ethynyl-17-Hydroxy-5(10)-Estren-3-One (Norethynodrel) and 17α-Ethynyl-19-Nortestosterone, Endocrinology 62:689 (May) 1958.
3. Rakoff, A. E.: Pages 800-805 of reference 1.
4. Tyler, E. T., and Olson, H. J.: Pages 704-709 of reference 1.
5. Kistner, R. W., Endometriosis, in Conn, H. F. (editor): Current Therapy—1959, *Philadelphia, W. B. Saunders Company, 1959, pp. 610-612*

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.

1960 Annual Meeting, *Miami Beach, Fla., June 13-17.*
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-Dec. 1.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 25-30.

AMERICAN

1960

January

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive *Secretary.*

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., *Jan. 28-30. Dr. William N. Valentine, U. of California* Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, *Williamsburg Inn,* Williamsburg, Va., Feb. 11-13. Capt. Lloyd B. Shone, Bureau of Medi*cine and Surgery,* Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, *Fla.,* Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, North Carolina Chapter, Hotel Barringer, Charlotte, N. C., Feb. 26-27. For information write Dr. Alexander Webb Jr., 201 Bryan Bldg., *Cameron Village, Raleigh,* N. C.

American College of Surgeons, Sectional Meeting for Surgeons and *Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3 For information write:* Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., *Phoenix, Ariz.,* Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. *John Hunton, 450 Sutter St., San Francisco* 8, Executive Secretary.

Central Surgical Association, *Drake Hotel,* Chicago. *Feb. 18-20* Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., *Chicago* 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. *Leslie H. Adams, 774 Adams Ave.,* Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben *Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.*

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

American Academy of General Practice, Philadelphia, Mar. 18-24. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Mo., Executive Director.

American Association for the History of Medicine, Inc., Charleston, S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Institution, Washington 25, D. C., Secretary.

American College of Surgeons, *Sectional Meeting,* The Broadmoor, Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H. P. Saunders. 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Portland Hotel. Portland. Ore., Mar. 28-30. *For information write: Dr. H. P.* Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, N Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., *Secretary-Treasu*

American Laryngological Association, Deauville Hotel, Miami Bea *Fla., Mar. 18-19. Dr. Lyman Richards,* Massachusetts Institute of Te nology, Cambridge 39, Mass., Secretary.

American *Laryngological,* Rhinological and Otological Soci Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Ste Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, F Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneap 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deau *Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barbe* Lane, Roslyn Heights, N. Y., Secretary.

American *Psychosomatic* Society, *Sheraton-Mount Royal Hotel,* Mo real, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N. Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Ri Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory U versity, Atlanta 22, Ga., Secretary.

Association of Clinical Scientists, DeWitt Clinton Hotel, Alba *N. Y., March 3-5. Dr. Robert P. MacFate, 54 W. Hubbard St., Chic* 10, Secretary.

Intermountain Pediatric Society, *Stardust Hotel, Las Vegas,* N Mar. 28-29. Dr. Joseph R. Newton, 2000 S. 9th East, Salt Lake C Utah, Publicity Chairman.

Missouri State Medical Association, Sheraton-Jefferson Hotel, Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Louis Executive Secretary.

National Health Council, National Health Forum, Miami, F *Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19,* Exe tive Director.

National Multiple Sclerosis Society, *New York City,* Mar. 8. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, N Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., N *Orleans 12, Executive Secretary.*

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, M *21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3,* Ga., Execu Secretary.

Southwestern Surgical Congress, *Riviera Hotel, Las Vegas,* Nev., M 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma C Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Sem Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jackson Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla., A 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Execu Secretary.

American Association of Anatomists, Statler-Hilton, New York C *Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy,* School of Medic Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, *Chicago,* Apr. 11-15. Calderon Howe, Columbia Univ. College of Physicians and Surge New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, H Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. *Holman,* D of Pathology, L. S. U. School of Medicine, New Orleans, La., Secreta

American Association of Railway Surgeons, Drake Hotel, *Chica* Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chicago Executive Secretary.

American College of Obstetricians and Gynecologists, Netherla Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardson, 79 *Monroe St., Chicago 3, Executive Secretary.*

American College of Physicians, Mark Hopkins & Fairmont, San Fra cisco, Apr. 4-9. Mr. *E. R. Loveland,* 4200 *Pine St.,* Philadelphia Executive Secretary.

American College of *Surgeons, Sectional Meeting, Hotel* Leamingt Minneapolis, Apr. 11-13. For information write: Dr. H. P. Saund 40 E. Erie St., Chicago 11.

American College of Surgeons, *Sectional* Meeting, Kahler Hot Rochester, Minn., Apr. 14. For information write: *Dr. H. P.* Saunde 40 E. Erie St., Chicago 11.

American College of Surgeons, West Virginia Chapter, *The Gre* brier, White Sulphur Springs, W. Va., Apr. 1-2. Dr. Ray E. Bur Grace Hospital, Welch, W. Va., Vice-President.

American *Dermatological* Association, Inc., Boca Raton Hotel, Bo Raton, Fla., Apr. 8-12. Dr. Wiley M. Sams, 308 Ingraham Bldg., Mia 32, Fla., Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. Da D.Sc., 9650 Wisconsin Ave., *Washington 14, D. C.,* Executive Secreta

American Proctologic Society, Shamrock Hilton Hotel, Houston, Texa Apr. 25-27. Dr. Norman D. Nigro, 10 Peterboro, Detroit 1, Secreta

American Public Health Association, Southern Branch, Memph Tenn., Apr. 13-15. Dr. L. M. Graves, Shelby County Health Depa ment, Memphis, Tenn., Chairman, Local Arrangements Committee.

American Society of Biological Chemists, Inc., Chicago, Apr. 11-1 Dr. Frank W. Putnam, Dept. of Biochemistry, Univ. of Florida, Gaine ville, Secretary.

American Society for Experimental Pathology, Pick Congress Ho Chicago, Apr. 11-15. Dr. J. F. A. McManus, Univ. of *Alabama* Me Center, Birmingham, Ala., Executive Secretary.

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PROGRESS IN THE MANAGEMENT OF LABOR AND DELIVERY

M. Edward Davis, M.D., Chicago

Advances in obstetrics and gynecology in the past 25 years have strikingly reduced the dangers to mother and baby during the birth process. Parent education is the most important part of modern prenatal care. Like other aspects of modern maternity care it can no longer be provided by the mother's physician alone but calls for the help of professional colleagues. During a period of 27 years at Chicago Lying-in Hospital it has been possible to maintain a rate of about 5% for abdominal deliveries without sacrificing the best interests of mother and baby. In certain patients the operation should logically be extended to complete cesarean hysterectomy, and a series of 400 such operations has been performed without mortality. The incidence of birth trauma resulting in perinatal mortality has decreased markedly, but breech presentation still poses a problem. Discovery of the cause of pre-eclampsia and eclampsia and reduction of the incidence of cerebral palsy and mental retardation still challenge the investigator.

A VERITABLE miracle has taken place in the management of childbirth since the inauguration of the Section on Obstetrics and Gynecology in the American Medical Association. Most of the phenomenal advances have occurred during the last quarter-century. In 1935 more than 60 mothers lost their lives in giving birth to every 10,000 babies; in 1958 fewer than 4 mothers in 10,000 failed to survive the reproductive process. Each year has seen a further reduction in maternal mortality. There has likewise been a marked reduction in the hazard of birth for the baby. Thus in 1935 more than 60 babies in every 1,000 deliveries failed to survive; in 1958 this figure had been reduced by more than half (fig. 1).

What are the factors which have made childbirth such a safe experience in such a short span of years? First I would credit the distinguished physicians who made the profession aware of the needless loss and crippling of mothers and babies in the birth process. The recognition of the problem was followed by widespread educational efforts throughout the United States under the auspices of the American Maternal Welfare Committee, the Children's Bureau, and numerous other agencies. Second, the marked acceleration in the movement of pregnant patients from their homes to hospitals for delivery, brought about by the necessities of war,

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Joseph Bolivar DeLee Professor and Chairman of the Department of Obstetrics and Gynecology of the University of Chicago and Chief of Service of the Chicago Lying-in Hospital.

Read in the Symposium on Childbirth—Progress in Management before the Joint Meeting of the Section on Anesthesiology, the Section on Diseases of the Chest, the Section on General Practice, the Section on Nervous and Mental Diseases, the Section on Obstetrics and Gynecology, the Section on Pediatrics, and the Section on Preventive Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 11, 1959.

provided safer environments for births. Third, the rapid advances of the medical sciences which contributed the antibiotic drugs, safe and speedy blood replacement, intelligently provided pain relief and anesthesia, and new knowledge concerning the physiology of mammalian reproduction made possible the prevention and intelligent treatment of many obstetric complications. Last, the education of physicians, nurses, and allied professions in the problems of modern maternity care provided the necessary trained personnel. All of these advances, and the increasing awareness of the public that childbirth can be disastrous to mother and baby and should concern all enlightened people, are responsible for the miracle which has been achieved.

A quarter of a century ago human reproduction was regarded as a pathological process, fraught with great danger to mother and baby. Was it any wonder that the founder of the Chicago Lying-in Hospital, Joseph Bolivar DeLee, in the preface to the seventh edition of his famous textbook, *Principles and Practices of Obstetrics,* said, "Can a function so perilous that, in spite of the best care, it kills thousands of women every year, that leaves at least a quarter of the women more or less invalided, and a majority with permanent anatomic changes of structure, that is always attended by severe pain and tearing of tissues, and that kills 3 to 5 percent of children—can such a function be called normal?"

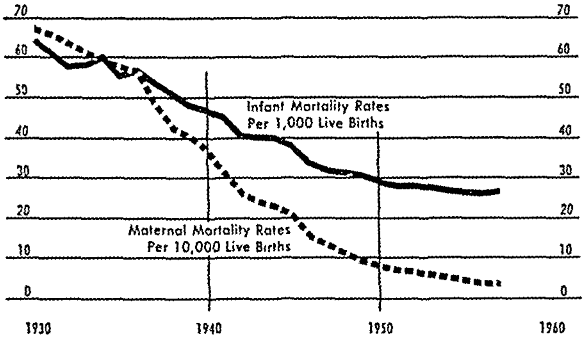

Fig. 1.—Maternal and infant mortality rates for the United States, 1930-1957, from Health and Vital Statistics, Washington, D. C., Public Health Service publication no. 600.

Is it any wonder that every aim and every effort were directed toward increasing the safety of being born for mothers and babies? Each new advance in medicine, all new knowledge, and every endeavor were directed toward this goal. As each additional safeguard resulted in a further reduction of maternal and fetal mortality, childbearing became ever more artificially encased in rigid techniques and practices. Slowly but surely every vestige of personal gratification, excitement, and emotional satisfaction in having experienced life's greatest reward was extinguished. The birth process was rapidly becoming one more marvel of mechanical efficiency so dear to the hearts of Americans.

Parent Education

The onset of labor represents the climax of nine long, eventful months. Modern maternity care should be designed in such a way that mothers are adequately prepared for this cataclysmic event. Intelligently given prenatal care will meet her changing physical needs and promote the normal growth and development of the baby. It should likewise attempt to meet the emotional needs of the mother, and the father too. How this can be best accomplished will depend on existing facilities. It can be carried out by the physician during periodic visits of his patient, if he realizes the importance of this facet of maternity care. The goal may be easier to attain in formal and informal discussion groups under the guidance of a nurse educator or some other person who has had special training in parent education. It may include posture exercises which have been designed to make the mother a more intelligent and cooperative participant and to decrease her discomfort in labor. The ultimate aim is education for parenthood, designed to remove the fears, the misinformation, and the taboos with which countless generations have surrounded the birth process.

Modern maternity care can no longer be provided by the mother's physician alone. In the first place, the doctor is much too busy to spend the time necessary to indoctrinate his patient in the many things that she should know. The expected avalanche of babies in the immediate future will overwhelm our profession. Furthermore, much of the care that the patient has a right to expect can be provided by a maternity nurse, a trained nutritionist, a medical social worker, and an anesthetist. These professional colleagues can and must assume an increasing responsibility in the field of obstetrics. Their special skills, properly utilized by the physician, can provide modern maternity care so necessary today and thus elevate human reproduction to the important place it deserves in our society.

Is parent education effective? Experiences at Chicago Lying-in Hospital and those at many other institutions have convinced me that it is the most important part of modern prenatal care. It has resulted in a marked decrease in the incidence of prolonged labor, a reduction in the need for analgesia, and fewer complicated deliveries. Preparation for labor will decrease the number of mothers admitted to our birth rooms in the premonitory phase, reduce the use of drugs at a time when they may alter the labor mechanism, and result in better patient cooperation. Most important, mothers will become enthusiastic participants in life's greatest adventure, and it can be a "labor of love."

Pain has been inextricably woven into the fabric of the birth process since the dawn of history. The third chapter of Genesis records the punishment of Eve and the mothers of mankind, "in pain shall you bring forth the children." Pain and uterine contraction have been synonymous in most languages of the world. On admission of the young mother to the labor room she is greeted by the questions: When did your pains start? How often do they recur? How long do they last? Pain, pain, pain; is there any wonder that much of our professional and scientific efforts has been directed toward the relief of pain, often at a price, for the mother and her newborn baby?

Education for childbirth can do a great deal to dispel the "curse of Eve." Knowledge of the labor mechanism, its physiological function, and its goal will remove much of the fear of the birth process and its dreaded sequelae. Uterine contractions can and do become uncomfortable and difficult to tolerate, but the timely and proper use of a host of drugs will relieve some of the discomfort and need interfere with neither the labor mechanism nor the establishment of normal respiration by the newborn infant.

Obstetric Operations Today

A more logical approach has been formulated to the delivery of the baby. Delivery through the birth canal is the most desirable objective; but it is no longer justified at any price. It is possible to evaluate the size of the pelvis rather accurately, and the final decision as to whether the baby can be delivered safely through the birth passages may await an intelligent test of labor. The length of the test of labor is less important today than a careful evaluation of progress. In the final decision to terminate the labor by cesarean section one should give careful consideration to the fact that, once a cesarean section is carried out, future deliveries will most likely be accomplished by the abdominal route. Thus the indication for the performance of the initial cesarean operation is of paramount importance for the patient's future childbearing.

The difficult forceps deliveries of the past have become less and less common. Certainly there is no proper indication for the application of forceps on the head that is not well engaged in the pelvis. The so-called high forceps delivery is a relic of that period of obstetric practice when delivery through the birth canal at any price was an achievement. The midforceps operation should be reserved for the patient who does not exhibit cephalopelvic disproportion, who has complete cervical dilatation, but in whom, once it has reached the midplane of the pelvis, the head fails to descend further because it remains in a posterior or transverse position. These moderately difficult forceps deliveries can be accomplished by the experienced physician with little hazard to the baby or its mother.

The incidence of traumatic deliveries has decreased tremendously. In the practices of most trained specialists and in many large teaching hospitals labor is often terminated by outlet forceps delivery after an adequate episiotomy, first described by DeLee over 40 years ago as "prophylactic forceps" delivery. This nontraumatic procedure has gained wide acceptance. However, patients can deliver spontaneously, preferably after an adequate episiotomy has been performed. The important consideration is that the trauma of the delivery be kept at a minimum.

The incidence of birth trauma resulting in perinatal mortality has also decreased markedly. At the Chicago Lying-in Hospital the perinatal death rate per 1,000 births during the period 1931 to 1941 was 5.34; in 1951 to 1956 this had been reduced to 0.7 (fig. 2). The hazard of fetal trauma can be further reduced by the intelligent management of labor, decrease in the incidence of prolonged labor, elimination of the injudicious use of analgesic drugs, and selection of the proper mode of delivery. The most critical period for the baby is labor and delivery. Fetal trauma can be prevented by gentleness in every manipulation, for no one can be certain that delicate vessels in the brain may not be stretched and ruptured. Every experienced physician has been shocked to learn that the easy uneventful delivery of a baby one, two, or three years previously may have been responsible for subtle damage and subsequent mental retardation.

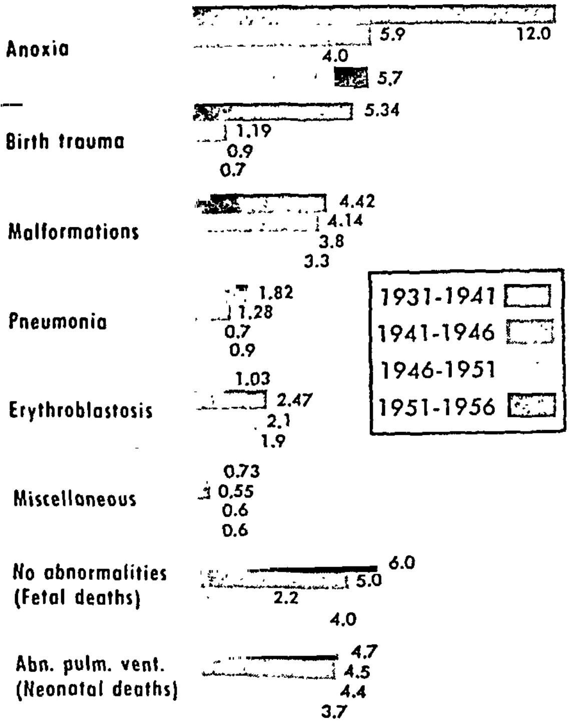

Fig. 2.—Fetal and neonatal deaths (infants weighing over 1,000 Gm.) at Chicago Lying-in Hospital, 1931-1956 (rate per 1,000 births).

The proper management of breech presentation may still pose a real problem. Although this presentation occurs in no more than 3 or 3.5% of all deliveries, it results in a disproportionately high incidence of perinatal mortality and, what perhaps is even more important, serious fetal damage but survival. It occasionally may cause more extensive damage than even the moderately difficult forceps delivery. I have suggested in my teaching that one approach to this serious problem is more frequent attempts at the external version of the polarity of the fetus from breech to cephalic presentation. Such a procedure, carried out in the last month of pregnancy and with great gentleness and a lack of persistence, will result in little hazard to the placenta or the cord. It can reduce the incidence of breech deliveries by more than 50%. However, external version has not gained popularity.

Breech delivery should be attempted only under the most ideal circumstances, for even the expert may meet unexpected complications. The general practitioner with little obstetric experience would serve his patient better if he sought more experienced help. Deep general anesthesia may be necessary, and its induction should not be relegated to an untrained nurse or casual assistant. Babies will fare better if labor is allowed to progress until the body is delivered to the umbilicus and then the completion of the delivery taken over by the attendant. Time has been overemphasized as a factor in successful breech delivery, for gentleness in all manipulations is a far greater safeguard to the welfare of the baby. The specialist often finds that use of forceps on the aftercoming head is less traumatic to the delicate brain than unbridled manual pressure from above in an attempt to force the head through the pelvis.

Cesarean Sections at Chicago Lying-in Hospital, 1931-1958

	May, 1931—March, 1942	March, 1942—July, 1949	August, 1949—July, 1958	Total, 1931—1958
Deliveries	29,290	27,360	31,786	88,436
Cesarean sections	1,500	1,371	1,572	4,443
Low cervical, %	92.0	89.0	79.4	86.5
Incidence, %	5.1	5.0	4.94	5.03
Maternal deaths, no.	10	2	2	14
Maternal mortality, %	0.6	0.15	0.13	0.31
Cesarean hysterectomy, %	6.4	10.7	20.5	13.4

Lastly, cesarean section deserves a more important place in the management of breech presentation. The older primigravida, the woman with a long period of infertility, the patient who fails to make consistent progress in labor, and the mother who has an unusually large baby all deserve consideration in the election of cesarean section. True, our incidence of cesarean section may rise a bit but the rewards will be many fewer dead or seriously damaged babies.

The Role of Abdominal Delivery

The role of abdominal delivery has been clarified in recent years. Early in the century it was a procedure resorted to in desperation when other methods of delivery failed. Needless to say, the risk for the mother as well as her baby were extraordinarily great. To reduce the hazard technical modifications of the operation were introduced, which improved the outlook somewhat. The development of the low or cervical cesarean and the extraperitoneal approach decreased the likelihood of infection and uterine rupture. However, it was the advent of antibiotics that increased the safety of abdominal delivery to the point where it has become a major approach for delivery in the face of complications.

There is no doubt that too many cesarean sections are being done today. However, an increased number of abdominal deliveries in the management of some of the complications will bring a real reward in the form of healthy undamaged babies. No one would question that version and extraction has become an obsolete procedure in the treatment of prolapsed cord and that timely cesarean section will save many babies and spare an occasional mother serious damage. Cesarean section, in the definitive treatment of placenta previa or for the premature delivery of the preeclamptic patient at a time when other methods of induction are not feasible, has provided rational and safe management for these serious complications. Perhaps a few additional abdominal deliveries are warranted in patients with large postmature babies, in women who in labor exhibit evidence of continued fetal anoxia, and perhaps to terminate an excessively long labor in a woman in whom progress is lacking. Properly selected indications need not increase the total incidence of cesarean section. During a period of 27 years at Chicago Lying-in Hospital we have been able to maintain a rate of about 5% and yet use abdominal delivery whenever necessary to the best interests of mother or baby (see table).

I should like to call your attention to complete cesarean hysterectomy as a logical extension of abdominal delivery. The diseased uterus is often better removed, in a woman approaching the end of her reproductive years. To postpone such a procedure until after delivery imposes another major operation on the mother, with its incidental inconvenience and small hazard. It is possible to remove the uterus completely at the time of delivery without increasing the risk to mother or baby. Since 1951 we have done more than 250 complete cesarean hysterectomies with no mortality and fewer complications than were exhibited in patients who had low or cervical cesarean section. This procedure is a logical advance in our management of abdominal delivery.

The Future

The future of obstetric practice will be shaped by new knowledge brought forth by the increasing tempo of research in mammalian reproduction rather than by improved technical skills. The well-trained clinician can manage labor and delivery superbly and safely. But what about many important problems which remain unanswered? Reduction in the high incidences of cerebral palsy and mental retardation has high priority. Toward this end we need to know more about human genetics, early environmental influences on the growing embryo, and the forces which control the transportation and utilization of oxygen from mother to fetus. An adequate oxygen supply during labor and delivery is the very lifeline of fetal survival and the means of prevention of subtle and serious brain damage. In the foreseeable future it should be possible to control the entire labor mechanism by new knowledge about the hormones which regulate the reproductive process. Such scientific developments will reduce the frequency of premature delivery, prolonged labor, and ineffective uterine mechanisms. The discovery of the cause of preeclampsia and eclampsia is within our reach. As the sciences push the frontiers of knowledge ever outward, we can look forward to our utopian tomorrow when human reproduction will be even more exciting, safe, and rewarding for parents, society, and our citizens of tomorrow.

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PRENATAL FACTORS IN INTELLECTUAL AND EMOTIONAL DEVELOPMENT

Albert S. Norris, M.D., Iowa City

Environmental factors effecting the intellectual and emotional development of a person have been fairly well delineated except for the period of fetal intra-uterine life. Certain mental diseases (epilepsy and mental deficiencies) are known to have etiological factors operative in the prenatal and delivery periods. Evidence here reviewed indicates that ill-advised choice of therapy during pregnancy can cause physical defects in the fetus. The likelihood exists that defects of the central nervous system can arise in the same way. If so, the obstetrician shares in the responsibility for preventing mental illness.

Psychiatry has long emphasized the importance of environment, often, unfortunately, to the exclusion of everything else. One area of environment, however, that has been almost completely ignored is that of the nine months of prenatal existence.

Earlier experiences usually have a greater influence on development than those occurring later, so it may be logical to assume that these first nine months, particularly the first trimester, may be the most significant period of our lives.

If we can pinpoint prenatal causes for at least some of the mental diseases, the epilepsies, and the mental deficiencies, then this places the obstetrician in a position to do preventive psychiatry.

That prenatal factors may influence the fetus has long been known and accepted. But some old and some more recent work has suggested that the ways in which the fetus may be influenced and the effects that these influences may have on it are much greater than we had thought.

Petersen [1] in 1933 published a paper relating the incidence of malformation to month of birth. With 100% taken as the normal expectancy, he found that children conceived in March and April had a 120% rate of malformation while those conceived in August and September had only a 70% rate. He related this to the fact that in the spring the weather was more irregular, and implied that somehow this was able to affect the germ plasm. This sounds like rather a fantastic conclusion, but, in the 1930's, he was not alone in relating weather to the health of infants and to many other medical conditions.[2] Huntington [2a] reviewed literally dozens of such concepts, including the observation that children born in June are more likely to enter mental hospitals than those born at other times. This is particularly clear in young schizophrenic patients (fig. 1).

Physical Trauma

Ingalls [3] in 1947 reviewed the literature on the etiology of mongolism and related this condition distinctly to prenatal influences. Not only was there a correlation between the aging mother and the

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incidence of mongolism, but also significant were gestational hemorrhage, threatened abortion, disorders of the uterus, and recurrent infection occurring about the second month. He believed that the crucial period was about the eighth week of fetal life, and he suggested that lack of oxygen for the fetus may be an important mechanism.

Lilienfeld and co-workers[4] and Pasamanick and co-workers[5] in the past few years have done a series of studies attempting to relate maternal and fetal factors to the development of cerebral palsy, mental deficiency, epilepsy, and behavioral disorders.

The mothers of 27.7% of white epileptic children studied had at least one complication of pregnancy, as compared to those of 18.8% of controls.[4a] In cerebral palsy the figures were 38.8 as compared to 20%.[4b] In evaluating mental deficiency the authors found a history of pregnancy complications in 34.4 as compared to 25.2% for the mothers of normal children.[5a] There was a similar pattern with behavior disorders; 33.3% among the problem children and 25.2% for the controls.[5b]

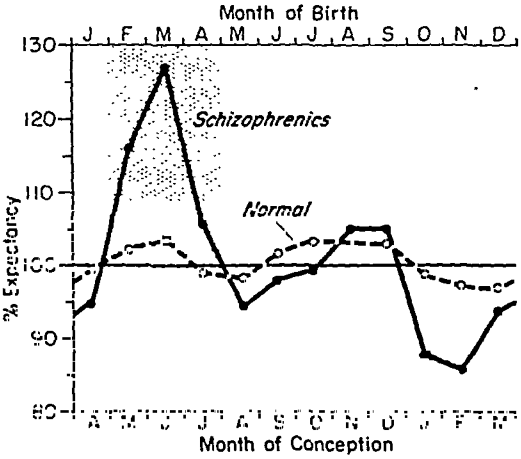

Fig. 1.—Incidence of disease in group of young schizophrenics, aged 14 to 23 years, showing variation with month of conception or birth. Extremes show 128% rate in those conceived in June compared with 84% rate in those conceived in January. Reprinted from Huntington[2a] with permission of John Wiley & Sons, Inc.

These figures certainly do not indicate that prenatal experiences explain all or nearly all of these conditions, but these differences are significant and must be accounted for. It was also found in these studies that nonmechanical abnormalities, such as bleeding during pregnancy and toxemia, appear to be much more important factors than the mechanical factors and complications of delivery which have often been blamed for these conditions. Knobloch and Pasamanick[6] postulated that there is a "continuum of reproductive casualty," resulting at its worst in fetal and neonatal death and when less extensive in brain damage producing cerebral palsy, epilepsy, behavioral disorders, and mental retardation. The concept of this continuum can be carried a bit further, and one might ask whether even lesser degrees of damage might occur which would be impossible to detect clinically but might predispose the patient to mental illness or emotional instability later in life.

Time of Conception

These authors also investigated the significance of time of birth (or time of conception) in mental deficiency. They found that persons conceived in June had an incidence of 1.57 per 1,000 while those conceived in December had a rate of only 1.29 per 1,000—a statistically significant difference. It is hypothesized that this occurs because mothers have a decreased protein intake during the summer and, if this protein deficiency occurs during the early months when cortical development and differentiation are occurring, brain damage will result. If mothers eat less protein-containing foods during the heat of summer, then we would expect a still lower intake during very hot summers and a subsequent increased rate of mental defectives conceived about that time. This in fact was found. When the median summer temperature was above average, the rate was 1.524 per 1,000 and when it was below average the rate was 1.295 per 1,000.

Since there is a seasonal variation in mental deficiency and since mental deficiency seems to be related to prenatal factors, there should be a seasonal variation in complications of pregnancy. It has been found that in pregnancies beginning in October, November, and December the incidence of complications is 6.4%, while in those beginning in April, May, and June the incidence is 8.7%.[7] The complication most closely related to spring pregnancies is eclampsia, which fits the protein-deficiency theory of eclampsia. Also significantly higher, however, are the complications of heart disease and uterine bleeding. The implications of these findings for the understanding and prevention of mental disease are of great importance.

There have been several studies relating anoxia to schizophrenia and other mental diseases.[8] One can see that anoxia in prenatal life may produce central nervous system damage, predisposing the person to emotional or mental trauma; or, more indirectly, cardiovascular damage might result from complications during the prenatal period, resulting in inadequate cerebral oxygen supply in later life. There is considerable evidence to indicate that persons with schizophrenia and some other mental disorders do have immature cardiovascular systems, and this is one of the theories of their etiology.[9]

Emotional Trauma

Thus far I have mentioned only the effects that the prenatal environment may have on the future emotional and intellectual development of the child. However, what of the mother's emotions during this period? Can they be one of the "complications" of pregnancy? We all know of the old wives' tales: "Martha was frightened by a rabbit and so little Henry was born with a harelip." This is about all that was known until quite recently.

Stott[10] in England set out to investigate a group of retarded children, but he included in his complications of pregnancy both physical and emotional factors. By emotional stress the author meant severe marital trouble, serious illness or death in the family, being bombed out, and similar "shocks." When these were added to the physical complications, the findings became more highly significant. Pregnancy illness, stress, or both were reported in mothers of 66% of the 102 retarded children but in only 30% of those of the 450 controls. He also correlated in this group the amount of prenatal complication with the amount of illness in the first 3 years of the infant's life. Here he found that, in cases where mothers reported illness or stress during pregnancy, 76% of the children developed a significant illness in their first 3 years. In those retarded children whose mothers had no pregnancy difficulty only 29% developed such an illness.

Recent work points out some convincing evidence for the relationship between environmental stress and the development of eclampsia. Salerno[11] examined 51 patients with toxemia of pregnancy. He divided these into those with preeclampsia or eclampsia and those with chronic hypertensive vascular disease. In the former group he found that most of the patients were under 25 years of age and were having their first children, and there were a number of unwed mothers. This was not true of the other group. He hypothesized that the factors of youth, primiparity, and unwed status may represent stress and result in a higher incidence of toxemia. When it is remembered that eclampsia is one of the causes of mental deficiency or fetal damage, this suggests a mediating factor between emotion and the development of the fetus.

Stott[12] also attempted to relate emotional and physical "shocks" in the pregnancies of mothers of defective children to their time of occurrence in the prenatal period (fig. 2).

There is a definite increased incidence of shocks in the early months, particularly in infants with mongolism. When it is remembered that cerebral development and differentiation are critical in the first 12 weeks, a possible cause and effect relationship can be seen.

If such nebulous things as emotion and time of conception can produce significant changes in the development of the fetus, what of the things that we as physicians do to pregnant patients? Almost nothing is known of this but there are occasional case reports that are suggestive, including the development of cleft palate in the child of a woman who received cortisone on the 38th day of pregnancy; the loss of a baby two years after transfusion; and the near loss 15 years after transfusion.[13] Many cases of minimal subclinical damage may be occurring, not becoming manifest until much later in life, and being called schizophrenia or neurosis.

Recently it has been shown that newborn mice and guinea pigs are not yet able to metabolize hexabarbitone and phenacetin.[14] What happens to the fetus when these and other drugs are administered to the mother? No one knows, but it is important to find out.

Work on prenatal influences is new and still very speculative. If these relationships are confirmed and expanded in the future, as I believe they will be, perhaps we can learn how to protect the fetus from the psychophysiological influences that emotional and physical stress exert. If so, the obstetrician may be placed in the first line of defense against mental illness.

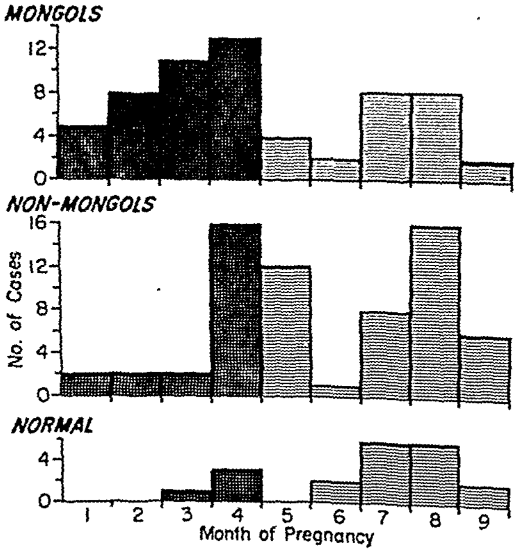

Fig. 2.—Incidence of "shocks" in prenatal period in children with mongolism, retarded children without mongolism, and normal controls. There is significantly greater number of "shocks" in groups of those with and those retarded but without mongolism. This is particularly clear in early months of those with mongolism. Reprinted (slightly modified) with permission of Stott[12] and *Journal of Psychosomatic Research.*

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TWENTY-FOUR-HOUR OBSTETRIC ANESTHESIA COVERAGE

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Two distinctive factors in obstetric anesthesia are the presence of a fetus and the frequent emergency nature of the anesthesia. Advances in this field, comparable to those in anesthesia for general surgery, depend on attracting an adequate number of anesthesiologists into it. This is more important at present than new drugs or new techniques. Experience here analyzed represents a period from 1945 through 1956 in a hospital where deliveries under some form of anesthesia numbered about 3,800 to 3,900 per year. The type of organization needed to insure good anesthesia includes a liaison committee of anesthesiologists and obstetricians who must meet regularly and deal with mutual problems as they arise. The anesthesiologists, obstetricians, hospital administrators, interns, medical students, and patients all need education about the need for and importance of good obstetric anesthesia, for the task of administering the anesthesia, like that of delivering the baby, requires the undivided attention of a trained physician.

Throughout America today obstetric and gynecologic services have been hindered in providing complete maternity service through serious shortages in anesthesia coverage. For the past two decades the rapidly developing science of anesthesiology, through a better understanding of physiology and pharmacology, has eliminated the hazards of extreme depths of narcosis and has helped surgeons open new vistas of progress in surgery. These two statements represent serious incongruities that can be explained only by eccentric placement of emphasis. I do not wish to minimize the advances made in conjunction with surgery, because the presence of these advances points out the importance of the subject matter. I would rather redirect some of the attention toward the challenges, requirements, and rewards of providing complete obstetric anesthesia coverage by day and by night.

General Considerations and Challenges

Of the more than 4 million births per year in the United States about 3 million, or 75%, are conducted with the aid of some form of analgesia or

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Read in the Symposium on Childbirth—Progress in Management before the Joint Meeting of the Section on Anesthesiology, the Section on Diseases of the Chest, the Section on General Practice, the Section on Nervous and Mental Diseases, the Section on Obstetrics and Gynecology, the Section on Pediatrics, and the Section on Preventive Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 11, 1959.

anesthesia, or both. This represents a little over 20% of the 14 million anesthesias induced each year in the United States. Two frequently forgotten factors in obstetric anesthesiology are the presence of a fetus and the frequent emergency nature of the anesthesia. Also to be considered is the challenge of the future, with the anticipated 50% increase in the number of births to 6 million by the year 1970. For the anesthesiologist the administering of anesthesia is not the only important consideration during labor and delivery. At times the withholding of anesthesia and the administering of supportive oxygen or intravenous blood or fluids or both is far more important to the maternal and infant welfare. Maternal and infant resuscitation are also important to the anesthesiologist. These functions, as well as assistance and support in the use of sympathetic and tranquilizing psychology, are the responsibilities of the anesthesiologist.

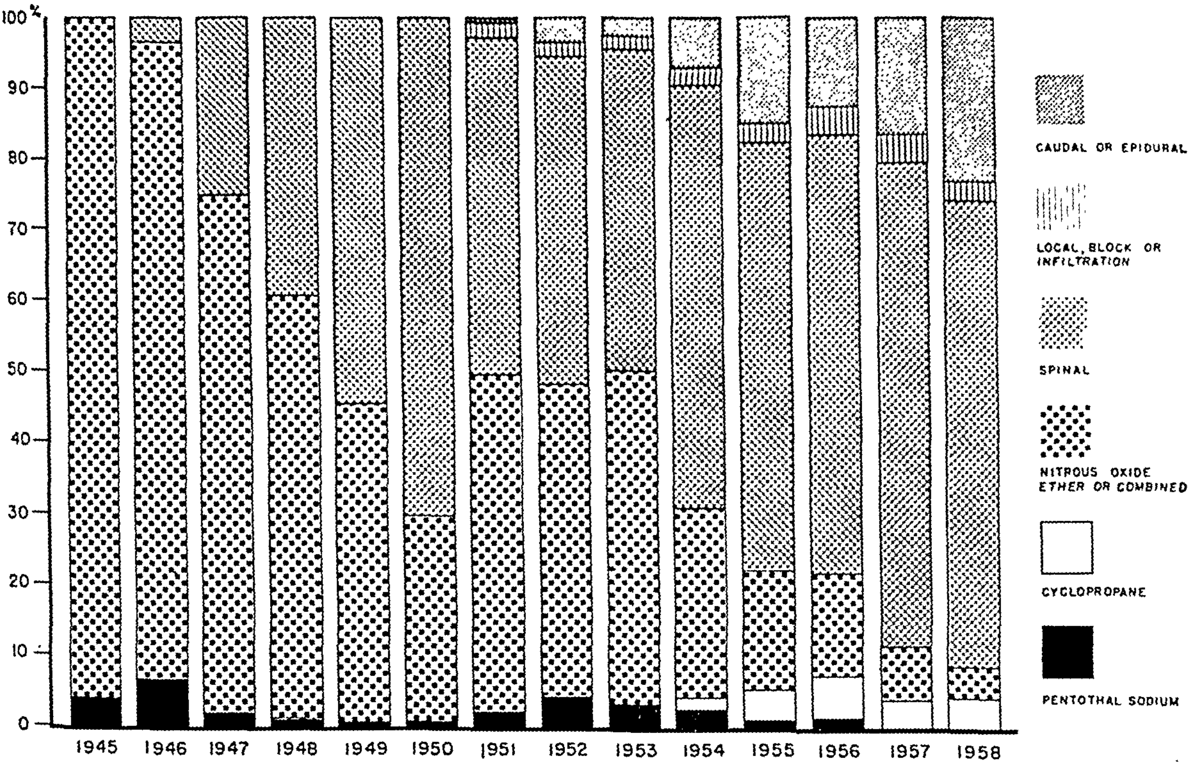

Fig. 1.—Techniques of anesthesia used at MacDonald House. In 1949 and 1950 sudden increase in spinal anesthesia was due *to occurrence of two anesthetic deaths, within short period of time, both due to aspiration of vomitus. Increase in conduction* anesthesia after 1954 was because we have been able to obtain more physician anesthesiologists for coverage of department.

Problems of Obstetric Anesthesia in the United States.—There has been spectacular progress during the past quarter-century in the reduction of maternal mortality. However, it has been estimated that about 10% of all maternal deaths in the United States are attributable to anesthesia; thus further reduction is possible, because almost all of these deaths may be considered preventable. Inhalation of vomitus is probably the greatest cause of these deaths, and with an expert in the field of anesthesiology administering the anesthesia this cause could be reduced to almost nil. Unfortunately the obstetric anesthesia is frequently administered by a neophyte or a completely inexperienced person rather than by an expert. At present it is impossible for all patients to have the care of experts, because when the number of board-certified anesthesiologists is divided by the number of hospitals, the quotient is about one-quarter of a man per hospital. If the membership of the American Society of Anesthesiologists is used, the result will be about three-quarters of a man per hospital. It will take time to correct this deficit, but we should start to make our move in partial redirection now. The progress will have to be evolutionary rather than revolutionary; however, it can be and has been done in some centers throughout the United States. Except for a few papers[1] on how to obtain anesthesia coverage, most of the writings in obstetric anesthesiology have compared techniques or drugs and their advantages and disadvantages. I do not wish to belittle the relative importance of drugs or techniques; however, the knowledge and ability of the anesthetist is the most significant factor, and the method used is secondary in importance. With this thought in mind I feel that any constructive idea on how to attract qualified anesthesiologists into the field of obstetric anesthesiology is far more important than new techniques or the introduction of new drugs. If we can attract an adequate number of interested anesthesiologists, a rapid advancement in the field will soon follow.

Obtaining Twenty-four-Hour Obstetric Anesthesia Coverage.—To attempt a detailed discussion on how to obtain 24-hour anesthesia coverage for obstetrics would consume too much time. Each of the papers previously mentioned presents a slightly different approach to the problem and from them departments in various parts of the country should be able to glean ideas which would be appropriate to their situation. The most recent of these papers [1e] appeared in the April, 1959, issue of *Obstetrics and Gynecology* and lists the other papers in its references. Each of the papers places great emphasis on the fact that any progress which has been made in achieving 24-hour coverage was not a one-sided affair. It was possible because of the close coordination and cooperation among the anesthesiologist, the obstetric and nursing services, and the hospital administration, each having in mind the maximum safety and comfort of the mother and her unborn child. The papers also stressed that the anesthesiologist was on first call for obstetrics and was in the hospital for the 24-hour period. Thus, it can be said that when all services conscientiously work together success is assured.

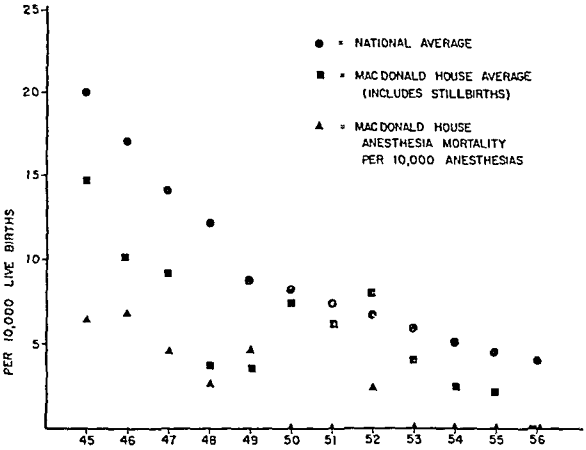

Fig. 2.—Maternal mortality. All anesthetic deaths have been due to patient's aspiration of vomitus while under general anesthesia. Aspiration death in 1952 resulted because resident in obstetrics insisted on deep ether anesthesia in patient with full stomach, despite objections raised by nurse anesthetist who was administering anesthesia.

I[1b] have found the following factors to be very important. 1. The physician anesthesiologist, like the obstetrician, should be dedicated to the idea of giving the best possible care to the mother and baby, by night as well as by day. 2. The anesthesiologist must be educated about the importance and need for the service and the important differences between obstetric and surgical anesthesia. 3. The obstetric staff and hospital administration must be educated about the need for the service and the improvement in patient care and service by physician "fee-for-service" anesthesia. 4. The patients have to be educated about the increased safety and better care for them and their babies. 5. The interns and medical students must be educated about the need and importance of the service and the professional and personal satisfaction they can obtain by rendering the service; as with every other specialty, here is the source material of the future specialist in the field. There must be organization, with adequate anesthesiologic personnel for the size of the service and with an equal distribution of duties and free time. The anesthesiologist must not exploit or be exploited, and his remuneration should be comparable to that of one in the private practice of obstetric or surgical anesthesia. There should also be a liaison committee, consisting of anesthesiologists and obstetricians, which meets to discuss mutual problems as they occur rather than permitting them to smolder. These meetings should take place at regularly stated intervals, so that the committee does not become defunct.

Experience of MacDonald House with Physician Anesthesiology

I would like to show our experience at MacDonald House with physician anesthesiology coverage. The period covered is from 1945 through 1956. The period 1945 through 1950 was covered by nurse anesthetists with the obstetrician administering his own conduction anesthesia. From 1951 through 1956 the coverage has been by physician anesthesiologists, with the assistance of nurse anesthetists. Each year there were approximately 4,000 deliveries with 3,800 to 3,900 of the patients receiving anesthesia of some from (fig. 1 and 2).

The Future.—The future progress of anesthesia in obstetrics will be assured when there is adequate coverage by trained anesthesiologists specializing in obstetric anesthesiology. This will relieve the obstetrician of the impossible task of both administering the anesthesia and delivering the baby, since each function requires the undivided attention of a trained physician.

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POSTNATAL PERIOD—GENERAL SCOPE

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The number of births in hospitals in the United States in 1957 was five times that in 1935. The average duration of the patient's stay in a maternity hospital has been shortened substantially, but it is probable that the lag in growth of facilities, the lack of personnel, and higher costs are in part responsible for the shorter stay. A shortage of professional nurses has necessitated increased use of auxiliary personnel. Early dismissal of the patient deprives her of some undeniable benefits of hospitalization and increases the responsibilities of the family physician. If the postpartum period is thought of as but one stage in the continuing health care which all women need throughout a lifetime, these trends should be viewed with concern.

When I was in medical school one of the requirements for graduation was that each student attend a certain number of home deliveries. Today, with 96% of births in the United States occurring in hospitals, I doubt whether such a requirement could be met, even if it were desirable. While the number of hospital patients of all kinds has about doubled in the past two decades,[1] births in hospitals have increased over 400% from less than 800,000 in 1935 to more than 4 million in 1957, an increase of about 3,250,000 mothers and more than 3,250,000 newborn infants in 22 years. In a recent survey of general hospitals[2] 22% of admissions were to the obstetric service. These were exceeded only by admissions to surgery, which accounted for 25%.

What has been the effect on hospitals of the rapid influx of maternity patients? Has the growth in hospital facilities and in numbers of professional personnel kept pace with the demand for maternity services since World War II? To obtain a partial answer to these questions data collected from several sources are compared for the years 1946 and 1957. A "fact sheet" of selected developments affecting maternity and newborn infant care in hospitals has been mimeographed and distributed (see table).

The number of maternity patients delivered in hospitals increased by 50% between 1946 and 1957 from 2,700,000 to 4 million. During the same period in general hospitals[3] the number of bassinets, which gives a general idea of the size and rate of expansion of maternity services, increased from 81,000 in 1946 to 96,000 in 1957, only an 18% increase. The net result is that the ratio of the number of bassinets to the number of births was actually smaller in 1957 than in 1946; namely, 226 bassinets per 10,000 live births in 1957 compared with 246 in 1946. Does this mean that for the nation as a whole expansion of maternity units has not been sufficient to meet the needs for hospital care of obstetric patients or that fewer facilities are needed because of shortened hospital stay?

Because of current migrations into and out of the central parts of cities, and because of the large increase of births to nonwhite mothers, hospitals in the same community may have differing needs for maternity beds. For example, some central city public hospitals are reported to be overcrowded, while the maternity census in central city private hospitals is going down and that of suburban hospitals is rising. In other areas an actual shortage of maternity beds may exist, because of a large industrial development or a military installation which attracts large numbers of men and women of childbearing age.

Since medical and nursing services are even more important than facilities in the care of patients, the availability of medical and nursing personnel is a major factor. Although the number of internships which were filled increased from 6,300 in 1946 to 10,200 in 1957, the ratio of interns to births has remained about the same, 23 or 24 per 10,000 live births. In spite of the increase in filled internships the disparity between the number of available intern positions and the number of graduates of American medical schools grows larger each year. In 1957, 5,000 or more internships were either vacant or filled by graduates of foreign medical schools.[1] In 1957 the American Hospital Association listed 6,818 hospitals,[3] yet only 867 hospitals were approved for training of interns in the year 1957-1958.[4]

Although the number of physicians in private practice is increasing, the population growth of the United States has been even greater; the ratio of physicians to population has been declining. In 1940 there were 108 physicians in private practice per 100,000 population; in 1949 there were 101 and in 1957 only 91.[5] The number of physicians in private practice in 1940 was 143,000; in 1949, 150,000; and in 1957, 156,000.[5]

What is the situation with regard to nurses? The number of nursing personnel employed in general hospitals is increasing—the number of professional

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From the Department of Health, Education, and Welfare, Social Security Administration, Children's Bureau.

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niques or the introduction of new drugs. If we can attract an adequate number of interested anesthesiologists, a rapid advancement in the field will soon follow.

Obtaining Twenty-four-Hour Obstetric Anesthesia Coverage.—To attempt a detailed discussion on how to obtain 24-hour anesthesia coverage for obstetrics would consume too much time. Each of the papers previously mentioned presents a slightly different approach to the problem and from them departments in various parts of the country should be able to glean ideas which would be appropriate to their situation. The most recent of these papers [1e] appeared in the April, 1959, issue of *Obstetrics and Gynecology* and lists the other papers in its references. Each of the papers places great emphasis on the fact that any progress which has been made in achieving 24-hour coverage was not a one-sided affair. It was possible because of the close coordination and cooperation among the anesthesiologist, the obstetric and nursing services, and the hospital administration, each having in mind the maximum safety and comfort of the mother and her unborn child. The papers also stressed that the anesthesiologist was on first call for obstetrics and was in the hospital for the 24-hour period. Thus, it can be said that when all services conscientiously work together success is assured.

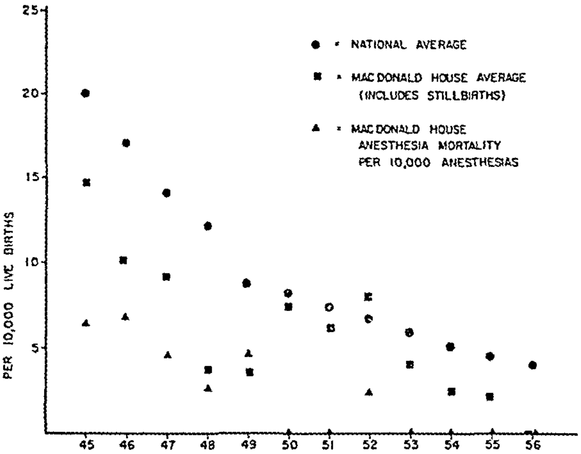

Fig. 2.—Maternal mortality. All anesthetic deaths have been due to patient's aspiration of vomitus while under general anesthesia. Aspiration death in 1952 resulted because resident in obstetrics insisted on deep ether anesthesia in patient with full stomach, despite objections raised by nurse anesthetist who was administering anesthesia.

I [1b] have found the following factors to be very important. 1. The physician anesthesiologist, like the obstetrician, should be dedicated to the idea of giving the best possible care to the mother and baby, by night as well as by day. 2. The anesthesiologist must be educated about the importance and need for the service and the important differences between obstetric and surgical anesthesia. 3. The obstetric staff and hospital administration must be educated about the need for the service and the improvement in patient care and service by physician "fee-for-service" anesthesia. 4. The patients have to be educated about the increased safety and better care for them and their babies. 5. The interns and medical students must be educated about the need and importance of the service and the professional and personal satisfaction they can obtain by rendering the service; as with every other specialty, here is the source material of the future specialist in the field. There must be organization, with adequate anesthesiologic personnel for the size of the service and with an equal distribution of duties and free time. The anesthesiologist must not exploit or be exploited, and his remuneration should be comparable to that of one in the private practice of obstetric or surgical anesthesia. There should also be a liaison committee, consisting of anesthesiologists and obstetricians, which meets to discuss mutual problems as they occur rather than permitting them to smolder. These meetings should take place at regularly stated intervals, so that the committee does not become defunct.

Experience of MacDonald House with Physician Anesthesiology

I would like to show our experience at MacDonald House with physician anesthesiology coverage. The period covered is from 1945 through 1956. The period 1945 through 1950 was covered by nurse anesthetists with the obstetrician administering his own conduction anesthesia. From 1951 through 1956 the coverage has been by physician anesthesiologists, with the assistance of nurse anesthetists. Each year there were approximately 4,000 deliveries with 3,800 to 3,900 of the patients receiving anesthesia of some from (fig. 1 and 2).

The Future.—The future progress of anesthesia in obstetrics will be assured when there is adequate coverage by trained anesthesiologists specializing in obstetric anesthesiology. This will relieve the obstetrician of the impossible task of both administering the anesthesia and delivering the baby, since each function requires the undivided attention of a trained physician.

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POSTNATAL PERIOD—GENERAL SCOPE

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The number of births in hospitals in the United States in 1957 was five times that in 1935. The average duration of the patient's stay in a maternity hospital has been shortened substantially, but it is probable that the lag in growth of facilities, the lack of personnel, and higher costs are in part responsible for the shorter stay. A shortage of professional nurses has necessitated increased use of auxiliary personnel. Early dismissal of the patient deprives her of some undeniable benefits of hospitalization and increases the responsibilities of the family physician. If the postpartum period is thought of as but one stage in the continuing health care which all women need throughout a lifetime, these trends should be viewed with concern.

When I was in medical school one of the requirements for graduation was that each student attend a certain number of home deliveries. Today, with 96% of births in the United States occurring in hospitals, I doubt whether such a requirement could be met, even if it were desirable. While the number of hospital patients of all kinds has about doubled in the past two decades,[1] births in hospitals have increased over 400% from less than 800,000 in 1935 to more than 4 million in 1957, an increase of about 3,250,000 mothers and more than 3,250,000 newborn infants in 22 years. In a recent survey of general hospitals[2] 22% of admissions were to the obstetric service. These were exceeded only by admissions to surgery, which accounted for 25%.

What has been the effect on hospitals of the rapid influx of maternity patients? Has the growth in hospital facilities and in numbers of professional personnel kept pace with the demand for maternity services since World War II? To obtain a partial answer to these questions data collected from several sources are compared for the years 1946 and 1957. A "fact sheet" of selected developments affecting maternity and newborn infant care in hospitals has been mimeographed and distributed (see table).

The number of maternity patients delivered in hospitals increased by 50% between 1946 and 1957 from 2,700,000 to 4 million. During the same period in general hospitals[3] the number of bassinets, which gives a general idea of the size and rate of expansion of maternity services, increased from 81,000 in 1946 to 96,000 in 1957, only an 18% increase. The net result is that the ratio of the number of bassinets to the number of births was actually smaller in 1957 than in 1946; namely, 226 bassinets per 10,000 live births in 1957 compared with 246 in 1946. Does this mean that for the nation as a whole expansion of maternity units has not been sufficient to meet the needs for hospital care of obstetric patients or that fewer facilities are needed because of shortened hospital stay?

Because of current migrations into and out of the central parts of cities, and because of the large increase of births to nonwhite mothers, hospitals in the same community may have differing needs for maternity beds. For example, some central city public hospitals are reported to be overcrowded, while the maternity census in central city private hospitals is going down and that of suburban hospitals is rising. In other areas an actual shortage of maternity beds may exist, because of a large industrial development or a military installation which attracts large numbers of men and women of childbearing age.

Since medical and nursing services are even more important than facilities in the care of patients, the availability of medical and nursing personnel is a major factor. Although the number of internships which were filled increased from 6,300 in 1946 to 10,200 in 1957, the ratio of interns to births has remained about the same, 23 or 24 per 10,000 live births. In spite of the increase in filled internships the disparity between the number of available intern positions and the number of graduates of American medical schools grows larger each year. In 1957, 5,000 or more internships were either vacant or filled by graduates of foreign medical schools.[1] In 1957 the American Hospital Association listed 6,818 hospitals,[3] yet only 867 hospitals were approved for training of interns in the year 1957-1958.[4]

Although the number of physicians in private practice is increasing, the population growth of the United States has been even greater; the ratio of physicians to population has been declining. In 1940 there were 108 physicians in private practice per 100,000 population; in 1949 there were 101 and in 1957 only 91.[5] The number of physicians in private practice in 1940 was 143,000; in 1949, 150,000; and in 1957, 156,000.[5]

What is the situation with regard to nurses? The number of nursing personnel employed in general hospitals is increasing—the number of professional

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From the Department of Health, Education, and Welfare, Social Security Administration, Children's Bureau.

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nurses increased from 140,000 in 1946 to 242,000 in 1957. Although this is a large increase in absolute number, the relative increase per 10,000 live births was only from 426 in 1946 to 569 in 1957. The size of this increase is rendered even less impressive when it is realized that, in 1957, of the 242,000 professional nurses 56,000 or nearly one-fourth were part-time workers. Since the number of hours nurses work part-time varies widely, full-time equivalents cannot be computed. According to the American Nurses' Association, "The gain [in professional nurses] is due largely to an increase in the number of part-time workers and the readmission of married inactive nurses. It does not correct the shortage of qualified nursing personnel." [6] Many part-time nurses are willing to work only certain days or certain hours and may not relieve the nursing shortage in some of the more critical areas such as on the night shift in nurseries for newborn infants where the actual nursing-care needs of infants are the same around the clock.

*Selected Developments Affecting Maternity and Newborn Infant Care in Hospitals**

	1946	1957	Percentage Change
Maternity patients delivered in hospitals, estimated number†	2,700,000	4,000,000	+50
Bassinets			
Number[3]	81,000	96,000	+18
Number per 10,000 live births	246	226	−8
Medical internships filled			
Number[4]	6,300‡	10,200	+62
Number per 10,000 live births	23	24	+4
Professional nurses			
Number[3]	140,000	242,000	+73
Number per 10,000 live births	426	569	+34
Practical nurses and auxiliary workers			
Number[3]	83,000	285,000	+243
Number per 10,000 live births	253	671	+165
Public health nurses			
Number§	21,000	29,000	+40
Number per 10,000 live births	63	68	+8
Expense per patient day			
All types of patients[3]	$9.39	$26.02	+177
Average length of stay, days			
All types of patients[3]	9.1	7.6	−16
Maternity patients[10]	...	4.5	...

* Number of live births registered in the United States (48 states and District of Columbia) in 1957 was 4,254,784; in 1946, 3,288,672; in 1945, 2,735,456.

† Based on data from the National Office of Vital Statistics for registered live births in hospitals in 48 states and District of Columbia. A plural set of births is counted as one delivery. It is assumed delivery of all plural sets occurred in hospitals.

‡ 1945 data.

§ American Nurses' Association. Facts About Nursing, 1958.

While the number of professional nurses has increased, the growth in practical nurses and auxiliary workers in general hospitals has been even more rapid; from 83,000 in 1946 the number increased to 285,000 in 1957, more than a threefold increase. In 1946 the ratio of professional to nonprofessional nurses in general hospitals was about five to three; by 1957 the ratio was reversed in favor of the nonprofessional nursing staff to approximately one professional nurse to 1.2 practical nurse and auxiliary worker.

Of the 285,000 practical nurses and auxiliary workers in 1957, 23% were practical nurses. About the auxiliary workers, who constituted about 77%, a bulletin of the National League for Nursing stated, "Among the variety of workers in patient care in hospitals and health agencies, the aide, or auxiliary worker, today is by far the most numerous. Trained on the job—in some hospitals for relatively simple duties, in others for much of the nursing of patients—aides carry important responsibilities in the care of hospitalized patients." [7]

Has this change in the ratio of professional nurses to practical nurses and auxiliary workers affected the quality of the hospital care of mothers and infants? Has it had any effect on patient satisfaction? Some recent studies of nursing in hospitals deserve serious consideration. From a study of nursing functions by the Division of Nursing Resources of the Public Health Service, Department of Health, Education, and Welfare, it was learned that the professional nurse during the last decade spent, on the average, only 18 minutes during an eight-hour period with each patient.[8] This is in marked contrast to what patients feel they need, because it was shown that the patient's satisfaction was related to the number of hours of professional nursing care available, not to total nursing care (professional plus nonprofessional).[9] The nurse's activities which are most important to the patient "involve human relations skills. These are best carried out as the nurse provides physical care for the patient, and thus the teaching of the patient is not as effective when it is scheduled for a specific time as when it spontaneously meets a need of the patient." [8] The patient wants to be treated as an individual person, wants an explanation of his care, and wants to be a partner in planning his care. It is thought that the insecurity which many hospitalized patients feel explains some of the more trivial complaints against hospitals and that if more support and counseling of patients by professional nurses were available, there would be fewer criticisms of hospital care by patients.

Hamilton [1] predicted that "the [professional] nurse's position [in the future] will require an increasing amount of skill, ability, intelligence, and judgment" as more functions are delegated to her by the physician. The absence of the physician during many hours of the day and night in itself constitutes a delegation of authority. Ideally this calls for an increased amount of nursing care by professional nurses. If, however, the proportion of nonprofessional nurses continues to increase, the professional nurse "must pass along to those less skilled . . . some of the duties she previously performed." Also, the increased use of auxiliary workers makes necessary the employment of highly qualified professional nurses to supervise and to provide in-service training for large numbers of relatively untrained hospital personnel.

Since patient care must be individualized and will always involve personal services and since medical care has become increasingly complex, it is not surprising that hospital costs are high. The expense per patient day in general hospitals rose from $9.39 in 1946 to $26.02 in 1957, an increase of

177%. From the standpoint of utilization of hospital services, high cost is in many cases a barrier to care.

The average length of stay in hospital is the only item which decreased between 1946 and 1957. The stay for all patients in general hospitals decreased from an average of 9.1 to 7.6 days, reflecting recent scientific advances in medicine and the use of more specific and more intensive therapy. For maternity patients the average length of stay in 1957 was even shorter—4.5 days.[10] In some large public hospitals the stay may be as short as 24 to 48 hours. In such cases it is probable that the lag in growth of facilities, the lack of personnel, and the high cost work together to shorten the length of stay.

Essentially, early discharge means shortening of the postpartum stay in the hospital. What is the effect of this on the mother and on the newborn infant? What are the psychological as well as the physical effects? I know of no large follow-up study which would give us the answer, although a few unpublished studies have been done and some are now in progress. I believe the basic questions are: Can the general hospital which is geared to the needs of patients with acute illness also meet the needs of postpartum mothers, the majority of whom are healthy young women undergoing a physiologic process? Can a program be developed for them which is constructive and which will promote not only their health but that of their family?

What are some of the benefits that the postpartum patient can derive from hospitalization? From the standpoint of physical safety the first few hours after delivery are the most critical for the mother and the newborn infant. In recognition of her need for constant observation and care some hospitals have established a "recovery" or "constant care" room. This provides a setting for continuous and concentrated medical and nursing care for a limited period; in some cases watchful care of the patient may be lifesaving.

A need common to all postpartum patients is rest. Can the busy hospital, with its noise and bustle, be made more restful? Some mothers, in an all-out effort to be good parents, tend to disregard their own needs for rest, recreation, and adult companionship. Helping them work out a satisfactory plan to be followed when they leave the hospital will ease future tensions and relieve fatigue.

The postpartum patient also needs support and counseling during an emotionally labile period—some physicians refer to the depressed feeling many mothers experience a few days after their delivery as the "gray" period. But most of all, the mother needs a supportive relationship with professional workers when she is adjusting to the new baby, for "the capacity for parenthood does not come automatically with the birth of a child."[11] Under the guidance of wise, understanding professional nurses her motherliness develops as she gains confidence in feeding and caring for her baby and as she learns to anticipate the next stages in his development.

The father needs help, too, for the whole family is involved in childbearing. Hargreaves said, "There is no change more drastic in its effects on all within the immediate family circle than the birth of a new human being."[12] The father's role is an important one because the support, security, and understanding he gives his wife will enhance her motherliness. When family problems (and all families have them) are dealt with constructively at this time, family unity is strengthened, whereas failure to find satisfactory solutions may mean family breakdown.

Early dismissal of the patient from the hospital increases rather than decreases the physician's responsibility to his patient, which is to obtain the same services for her in the community that the hospital would give; specifically, the services of a public health nurse to supplement his own, and, if relatives are not available, the services of a homemaker, for early ambulation is not synonymous with early ability to resume household duties and care of the family. Health workers are becoming increasingly aware of the contribution that a homemaker can make to families with health problems. In recognition of this, the A. M. A. was one of the sponsors of a National Conference on Homemaker Services held in Chicago in February, 1959.

Increasingly, the postpartum period is being thought of not as the end of medical care for the mother but as one stage in the continuing health care which all women need throughout a lifetime. For the young woman who is at the beginning of the reproductive period, it is an opportunity for preconceptional guidance. Women at the end of the childbearing period deserve a careful evaluation, because with the average life expectancy of women being almost 74 years, they can anticipate many more years of good health and activity. The opportunity for prevention of fetal or neonatal death or a damaged or malformed child in the "high risk" woman who has already produced one or more perinatal casualties is an exciting new challenge. For this group the prenatal period is already too late to prevent many tragedies. Even though many causes of pregnancy wastage are unknown, some preventive measures are possible. As Nesbitt said, "It is not always necessary to know the finite causes of disease or death in order to take effective measures to control them. Maternal toxemia is a classic example of this. . . . If man's physical and social environment can be altered favorably, a preventive health program is practical whether or not the basic cause is understood."[13]

Some years ago I was asked to answer a letter addressed to the "Health Department" from a mountain man. It read, in part, as follows: "Dear Sir: I am writing to ask your advice. I want some personal advice and not just some little papers or pamphlets." He went on to say that when his wife had given birth to their first and second children she had got up in a day or two and begun helping him in the fields. Then he related what happened to her in each successive pregnancy—her third, fourth, and fifth; her sixth ended in a miscarriage. By the end of the first page she had had nine pregnancies. In her 10th she had a convulsion, then followed her 11th, 12th, and 13th. And now she was pregnant for the 14th time. She didn't want to do anything except lay around all the time. He didn't know whether she was getting lazy or not. He had heard when women had grown children they liked to sit down and let their children wait on them. The letter ended with the question, "Can it be that my faithful wife don't want to help me anymore?"

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TRANSFER OF VITAMINS FROM MOTHER TO FETUS

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The concentrations of vitamin B_{12} in serum obtained from the umbilical cord blood in 25 fetuses were compared with concentrations found in corresponding samples of maternal serum at the time of delivery. In every case the concentration in the fetal serum was higher than that in the maternal serum. This suggested an active transfer or drawing of vitamin B_{12} from the mother into the fetus. In 14 pregnant women, most of them in active labor, the intramuscular injection of crystalline vitamin B_{12} resulted only in a temporary elevation of the vitamin B_{12} concentration in the maternal blood above that in the fetal blood; after six hours the fetal levels were again higher than the maternal. Other data reviewed here indicate likewise that the fetus draws certain nutriments from the maternal source; this applies to certain vitamins and iron but not to glucose or inulin.

Pregnancy imposes a nutritional stress on the mother through withdrawal, by the fetus, of nutritional requirements from the maternal reserves. The object of this communication is to present data on and discuss the physiological importance of the concentrations of various water-soluble vitamins, namely, vitamin B_{12} (cyanocobalamin), ascorbic acid, vitamin B_6 (pyridoxine), as well as other nutrients, such as iron and glucose, in fetal and maternal bloods. For comparison, a physiologically inert substance, such as inulin, also was included in the study.

Transfer of Vitamin B_{12}

Vitamin B_{12} is essential in human nutrition and in the maintenance of health. A wide variety of experimental animals, when placed on a low-vitamin B_{12} diet, develop deficiencies in their reproductive

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processes and a severe growth deficiency in their young. No similar observations have been made in human beings, in whom a severe vitamin B_{12} deficiency is rare and in whom it has not been induced experimentally by dietary deprivation. Nevertheless, it seemed of interest to ascertain whether pregnancy induces abnormal metabolism and a greater utilization of vitamin B_{12}. Some observations on this topic, collected primarily as the collaborative effort of the department of biochemistry of the School of Hygiene and Public Health and the department of obstetrics of the Johns Hopkins Hospital, are reported below.

Decrease in Vitamin B_{12} Serum Level with Pregnancy.—The serum level of vitamins may be considered an index of tissue saturation. It may be assumed that a low vitamin B_{12} serum level reflects poor tissue reserve of this vitamin. On the other hand, elevated levels of that vitamin may be totally irrelevant to tissue saturation in certain diseases such as leukemia [1] or liver diseases,[2] in which the destruction of tissues to which vitamin B_{12} is bound takes place.

Heinrich,[3] Okuda,[4] and Boger and associates [5] have shown that vitamin B_{12} serum levels decline during pregnancy and that, as pregnancy advances, serum concentrations fall progressively to levels well below those observed in nonpregnant women. Young and co-workers [6] studied the vitamin B_{12} serum level of a group of pregnant women during the greater part of their gestation period. They reported that the drop in the levels was most marked toward the end of pregnancy and that it required a daily supplementation by 100 mcg. of vitamin B_{12} in capsules, or 25 mcg. of vitamin B_{12} coadministered with D-sorbitol, to maintain the prepregnancy level.

Similarly, studies with laboratory animals demonstrated that, at the time of delivery, the vitamin B_{12} content in the liver of pregnant rats was severalfold lower than that of nonpregnant rats, in spite of the fact that both the pregnant and nonpregnant rats had been given a stock diet containing liberal amounts of whole milk and desiccated liver, both rich sources of vitamin B_{12}. These data support the premise that low vitamin B_{12} serum levels indicate a depletion of vitamin B_{12} reserve.

Comparison of Vitamin B_{12} Serum Level of Fetal and Maternal Blood at Delivery.—There are several communications [7] which report that the vitamin B_{12} serum level of the maternal blood is considerably lower than that of nonpregnant women of comparable age and markedly lower than that of the fetal level. The results of one of our several studies are presented in figure 1. In this figure the vitamin B_{12} serum values of mothers are plotted as the abscissa against those of the fetal cord serums as the ordinate. Any maternal values neither larger nor smaller than the fetal ones would appear as points on the theoretical line drawn at an angle of 45 degrees. In every one of the 25 cases we studied the level of the cord serum was at least equal to, or in excess of, the vitamin B_{12} serum level of the mother.

These findings suggest that vitamin B_{12} is drawn from the mother to the fetus. These data corroborate our previous findings [8] that a large percentage of radioactive vitamin B_{12} injected into pregnant rats is transferred to the fetus. The rate of transfer of injected nonradioactive vitamin B_{12} to pregnant women through the placenta and finally to the fetus was also studied. In this study,[9] 14 pregnant women were each given 100 mcg. of crystalline vitamin B_{12} solution by intramuscular route from 1 to 22 hours before delivery. Most of the women were in active labor when they received their injection. Some of these women were delivered per vaginam and others by elective cesarean section. The maternal and fetal vitamin B_{12} serum levels, determined at the time of delivery, are shown in table 1. These data show that, when vitamin B_{12} was injected less than four to six hours before parturition, the maternal levels were higher than the fetal levels. However, when the vitamin was injected more than six hours before parturition, the fetal levels were higher than the maternal levels.

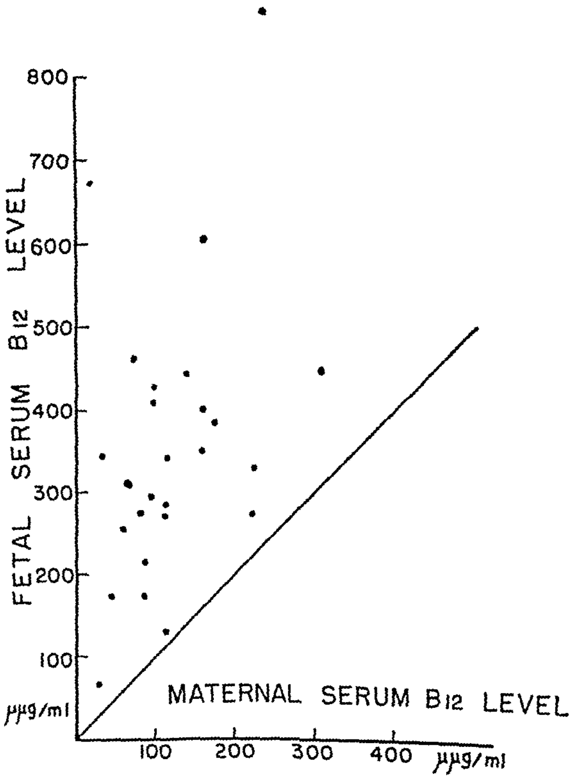

Fig. 1.—Maternal and fetal serum levels of vitamin B_{12}.

Physiological Significance of Low Vitamin B_{12} Serum Levels in Pregnancy.—Patients with pernicious anemia, in relapse resulting from inadequate absorption of vitamin B_{12}, infestation by a parasite, or dietary insufficiency, possess extremely low vitamin B_{12} serum levels. It is of interest to ascertain whether the low vitamin B_{12} serum levels resulting from pregnancy are of any physiological or clinical importance and, if so, whether daily supplements of vitamins should be given to all pregnant women.

TABLE 1.—*Patient Response to Vitamin B_{12} Given Intramuscularly Immediately Prior to Parturition*

Hr. Between Vitamin B_{12} Injection and Parturition	Vitamin B_{12} Serum Level at Parturition, μμg/Ml. Mother	Fetus	Difference*
1.0	1,700	575	+1,125
1.7	1,350	475	+ 875
3.0	1,325	800	+ 525
3.0	825	500	+ 325
3.0	1,000	800	+ 200
3.5	1,050	525	+ 525
3.5	1,050	575	+ 475
4.0	1,600	1,400	+ 200
4.0	1,075	1,375	− 300
6.0	750	1,125	− 375
6.0	775	500	− 275
7.5	500	700	− 200
12.0	800	1,275	− 475
22.0	650	1,100	− 450

* Plus sign indicates mother's level higher than that of fetus; minus sign indicates fetus' level higher than that of mother.

Data to answer these pertinent questions are lacking, and the purpose of the present discussion is merely to determine whether the biochemical signs of vitamin B_{12} deficiency, like the diet-induced deficiency in animals or the deficiency in patients with pernicious anemia, manifest themselves in the blood of pregnant women. Two of these established biochemical indicators are the decrease in the glutathione (GSH) content in the erythrocytes and a similar decrease in the glucose-ribose enzyme (GRE) which degrades glucose to ribose. Prystowsky and associates[9] reported that the glutathione content in the erythrocytes of maternal blood was lower than that in fetal red blood cells or in the erythrocytes of nonpregnant women. The values obtained for glutathione in the erythrocytes of maternal, fetal, and nonpregnant subjects were 203±10, 280±15, and 274±12 μM per 100 ml. of red blood cells respectively (table 2). The consistency of the maternal-fetal glutathione relationship is shown in figure 2, with fetal levels lower than those of the mother occurring in only 3 out of 24 cases. Hence, the difference is statistically significant.

TABLE 2.—*Comparison of Levels of Various Components in Fetal and Maternal Bloods*

Component	Unit of Measurement	Sources of Blood Fetal	Maternal	Non-pregnant
Glutathione (GSH)	μM/100 ml. RBC	280±15	203±10	271±12
Glucose-ribose enzyme (GRE)	Units*	310	190	268
Vitamin B_{12} binding substance	μμg/ml. serum	2.75±0.08	3.41±0.05	3.62±0.09

* Increase in ribose.

In contradistinction to the results obtained in the above two assays were the values obtained for vitamin B_{12} binding substance. The level of the binding substance in fetal serums almost always was lower than that in the maternal serums, 2.75±0.08 and 3.21±0.05 micromicrogram, respectively, of vitamin B_{12} bound by each milliliter of serum.

In a similar manner, Ranke and Chow[10] demonstrated that the glucose-ribose enzyme content of the erythrocytes of maternal blood is lower than that of the red blood cells of fetal blood or that of nonpregnant women (table 2). This enzymic activity apparently is correlated to the low glutathione content, since its activity could be elevated on addition of glutathione in vitro.

Aside from these biochemical changes, it may be mentioned that, since the original report of Okuda and associates[1] on the possible association between cretinism and a low fetal vitamin B_{12} serum level, a total of four cases of cretinism have been discovered in the Johns Hopkins Hospital. In all cases, the vitamin B_{12} serum level was immeasurably low. To the best of our knowledge, no congenital cretins have been reported on whose serum levels were normal. These data led us to believe that the markedly decreased maternal vitamin B_{12} serum levels are not as significant as the decrease of fetal vitamin B_{12} serum levels with respect to cretinism.

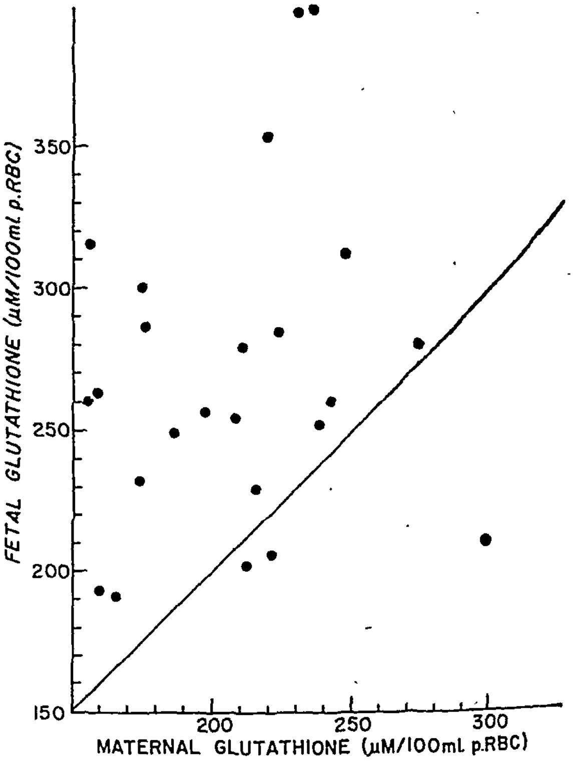

Fig. 2.—Maternal and fetal serum levels of glutathione (GSH).

Vitamin B_{12} Reserve and Parity.—If the maternal vitamin B_{12} reserve actually is depleted during the period of gestation, one may expect a rapid succession of pregnancies to result in depletion of the maternal reserve, which might manifest itself by a decrease in the vitamin B_{12} serum level and the vitamin B_{12} of the content of the liver. In a preliminary study with rats, one group of normal female animals was mated. After delivery, they were allowed to feed their young for 21 days and immediately were mated again. This process was repeated until these rats had given birth to four litters. The second group of animals was given a rest period of seven weeks between each pregnancy and, therefore, gave birth to their second litters when the first group of animals gave birth to their fourth litters. The third group of animals was not mated and served as a control.

After the first group had given birth for the fourth time, the animals were sacrificed and their serum and hepatic vitamin B_{12} levels determined. The findings demonstrated that the animals in the first group had low vitamin B_{12} levels in serum or liver and that they had progressively smaller young with each pregnancy. The animals in the second group had vitamin B_{12} reserves only slightly different from those of the third group. The size of their young as well as the number appeared to be reduced on rapid succession of pregnancies. It should be mentioned that the stock diet on which these animals were placed during the entire experimental period contained 1% desiccated liver, 25% whole milk, and 15% skimmed milk, all of which are rich sources of vitamin B_{12}.

TABLE 3.—*Number of Parity and Vitamin B_{12} Serum Level, Micromicrogram per Milliliter*

	Parity			
Country	0	3	10	15
U. S. A.	270±19	171±22	...	...
Foreign	198	158	110	100

A similar effect of parity on the vitamin B_{12} serum levels of pregnant women was reported by Young and co-workers.[6] They found a decrease in the vitamin B_{12} serum level with each successive parity. Their results, together with our recent data obtained from a study in the Philippines, are given in table 3.

Maintenance of Vitamin B_{12} Serum Level with Exogenous Vitamin B_{12} During Pregnancy.—Since the vitamin B_{12} serum level decreases during pregnancy, it becomes of paramount interest to determine the amount of vitamin B_{12} which must be given by mouth to maintain serum levels. To this end, five groups of pregnant women from the obstetric clinic of the Johns Hopkins Hospital were selected randomly and offered the following daily treatments: (1) no vitamin B_{12}, (2) 10 mcg. of vitamin B_{12}, (3) 100 mcg. of vitamin B_{12}, (4) 5 mg. of folic acid, and (5) 10 mcg. of vitamin B_{12} and 5 mg. of folic acid. In addition, all subjects received one daily capsule containing the crystalline vitamins except for B_{12} and folic acid. Vitamin B_{12} serum levels were obtained from these subjects at regular intervals.

Our results (table 4) show that the vitamin B_{12} serum levels of the subjects in groups A, B, and D declined as pregnancy advanced. However, when vitamin B_{12} was administered in doses of 100 mcg. the vitamin B_{12} serum was maintained at the initial level. It is interesting to note that, while administration of folic acid alone does not retard the decline in the vitamin B_{12} serum level, the combination of vitamin B_{12} and folic acid appears to maintain the vitamin B_{12} level of pregnant women. It should be pointed out that our results show that a large quantity of vitamin B_{12} must be given to maintain the serum level. This does not mean, however, that the daily requirement of vitamin B_{12} is 100 mcg., since only a small portion thus given is absorbed.

TABLE 4.—*Vitamin B_{12} Serum Levels of Pregnant Women with Various Vitamin B_{12} Therapies*

			Weeks of Gestation		
Treatment	Vit. B_{12}, Mcg.	Folic Acid, Mg.	15, Initial	27	40
A	0	0	337	131	116
B	25	0	281	211	197
C	100	0	297	220	232
D	0	5	240	143	115
E	25	5	322	310	263

Transfer of Other Nutrients

To ascertain whether the unusual relationship between the maternal and the fetal serum level of vitamin B_{12} is unique and specific, levels of other water-soluble vitamins were determined in patients from the ward of a general hospital in the Philippines. The maternal levels were compared with the fetal levels. The results of this study are given in table 5. It can be seen that in all instances the fetal level always was higher than the maternal level. It became of extreme interest to establish whether this selectivity is physiological or physiochemical. To this end, another group of pregnant women each were given an oral dose of glucose or inulin, from 1 to 24 hours before delivery, but similar gradient differences were not observed. It

TABLE 5.—*Comparison of Concentration of Various Nutrients in Fetal and Maternal Blood*

	Blood		
Component	Fetal	Maternal	Non-pregnant
Vitamin C	210	43	100
Vitamin B_6 (SGO-T)*	220	120	100
Vitamin B_{12}	130	60	100
Iron	150	67	100
Glucose	90	110	100
Inulin	100	120	100

* SGO-T reflects vitamin B_6 sufficiency.

should be pointed out that the molecular weight of glucose and inulin is of the same order of magnitude as that of ascorbic acid or pyridoxine.

The above data suggest that the fetus has a tendency to draw various vitamins but not glucose or inulin from the mother. We became interested in determining whether the serum iron level likewise differs in mother and fetus; the results indicate that the fetal serum level of iron, like that of vitamins, is considerably higher.

The above data, taken as a whole, clearly indicate that during the period of pregnancy the fetus draws its supply of various vitamins from the maternal source. This parasitic action applies also to iron but, interestingly enough, not to glucose or inulin. Therefore, it became of interest to determine whether the daily administration of a commercial source of prenatal vitamin preparation to pregnant women for one month or more prior to delivery would increase materially the various vitamin concentrations of the maternal as well as the fetal blood during parturition. The data presented in table 6 indicate clearly that daily treatment with this particular preparation, which contains unusually high levels of vitamins, raised the various vitamin levels studied.

TABLE 6.—*Effect of Daily Administration of Vitamin Supplement on Concentrations of Some Components of Maternal and Fetal Blood at Parturition*

	Vitamin B_{12}* µµg/Ml.		Transaminase, SGO-T Units/Ml.		Ascorbic Acid, Mg./Ml.	
Group	Cord	Mother	Cord	Mother	Cord	Mother
Vitamin supplement	260	170	18	12	21.7	13.6
Without vitamin supplement	197	120	11	8	11.8	8.7

* Stuart prenatal capsules were supplied by the Stuart Company, Pasadena, Calif

Summary and Conclusions

Although vitamin B_{12} (cyanocobalamin) is essential for the maintenance of health, its physiological role in humans is still a topic of further study. The data presented in this communication demonstrate that pregnancy imposes a nutritional stress on the mother through withdrawal by the fetus of vitamin B_{12} and other vitamins from the maternal reserves. As a result of this phenomenon, the maternal reserves, at least for vitamin B_{12}, decrease considerably, as evidenced by (1) the decrease of the vitamin B_{12} serum level in pregnant women, (2) the rapid transfer of a substantial amount of injected radioactive vitamin B_{12} in pregnant rats, (3) the decrease in hepatic and serum vitamin B_{12} levels during pregnancy, and (4) the two generally accepted biochemical criteria of vitamin B_{12} deficiency: namely, the decrease in glutathione (GSH) and the enzyme activity to degrade glucose to ribose, in the erythrocytes of pregnant women. Taken as a whole, these data indicate that vitamin B_{12} may be of physiological importance during pregnancy. Supporting data also are obtained from our observations that vitamin B_{12} serum concentration in the fetal cord blood of cretins is low. Furthermore, successive pregnancies lower the vitamin B_{12} serum level of pregnant women and the hepatic vitamin B_{12} reserve of rats.

It is interesting to note that the fetus, despite its initially higher levels of concentration, has the capacity to draw not only vitamin B_{12} but other vitamins such as ascorbic acid, B_1 (thiamine), and B_6 (pyridoxine), and also nutrients such as iron from the mother. If this phenomenon were one of a physiochemical nature, one might expect glucose and inulin to be divided in a similar manner between fetal and maternal blood. This, however, was not the case in our study. Furthermore, the work of Migeon and associates[11] indicated that maternal blood contained more 17-hydroxycorticosteroids than fetal blood. Thus, taken as a whole, these data would indicate that the differences in the vitamin B_{12} serum gradient will have physiological meaning and specificity and that this phenomenon is not primarily a chemical one.

615 N. Wolfe St. (5) (Dr. Chow).

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THE PLACENTA AND THE FETUS

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and
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An attempt was made to detect possible relationships between abnormalities in the placenta and subsequent aberrant growth in the infant. In a series of 654 deliveries, 262 placentas (40%) showed infarcts, fibrinoid degeneration, areas of old or recent abruption, and other malformations or variations. The corresponding 262 infants were compared with the 392 infants born with normal placentas. The differences showed that abnormality of the placenta increases the probability of nutritional disturbances in the first six months of postnatal life. Gross examination of the placenta can forewarn the physician of some common problems in the immediate postnatal period.

The well-being of the newborn infant depends not only on its genetic endowment but also on its mother's health and management through pregnancy, labor, and delivery. The formation, function, and senescence of the placenta and its role in maternal and fetal welfare are attracting increasing attention.[1] Malformations of the placenta have been identified with an increased incidence of abortion, premature birth, stillbirth, and bleeding in pregnancy for many years. However, placental function and anatomic changes during the third trimester remain under scrutiny and debate.[2]

Structural changes in the term placenta are common[3] and are said to be more common and more severe in many complications of pregnancy.[1] Measurements of placental function show similar alteration, particularly in reduced rates of radiosodium (Na^{24}) clearance from the placental pool.[5] Since the structural alterations seen are, in part, vascular, and since Na^{24} clearance is a measure of vascular function, it would be meaningful to establish a firm relationship between the two. However, at the present time, such a relationship from the fetal point of view can be considered only hypothetically. Complexity is lent to the problem of understanding maternal-placental-fetal relationships by the uncertainty of the physiological meaning to the fetus of placental structural variations and of differentiating between normal and abnormal, whether by physiological, gross anatomic, or histological means. Contemplation of cause and effect relationships becomes even more perilous when one recalls, on the one hand, that both the placenta and the fetus are conception products of similar derivation and, on the other, that current opinion links together complicated pregnancies, placental variations, and fetal problems.

Materials and Methods

The current study was conceived after observing markedly aberrant growth patterns in several infants born with placentas grossly variant in structure.[6] On the hypothesis that these growth aberrations were the result of prenatal deflections from the genetically determined pattern, we observed the conception products of all deliveries at the University of Missouri Medical Center between July 1, 1956, and July 1, 1958. These deliveries were classified into either a study or a control group, depending on placental descriptions. The study group was composed of those deliveries in which the placentas were noted to have infarcts, fibrinoid degeneration, areas of old or recent abruption, degeneration of cotyledons, loss of large crescents of the edges, and severe malformations. The control group was composed of the rest of the deliveries.

Maternal Population and Incidence of Placental Variations.—There was a 40% incidence of placental variation in all 654 patients delivered. Of Caucasoid patients 38% had variant placentas and of Negroid patients 44% had variant placentas. The distribution of study (87) and control (183) placentas among the Caucasoid private and clinic patients was significantly different, however, and the figures for private Negroid patients are too small to allow comparisons to be made. When the indigent Caucasoid and Negroid patients are compared, the respective rates of placental variations are 47 and 44%.

Premature Infants.—The incidence of prematurity for all patients was 6.9%; 4.4% for Caucasoid and 12.7% for Negroid patients. The variations seen in placentas in these cases, in addition to the common marks of senescence, were remarkable smallness, thinness, fibrinoid replacement, severe placenta circumvallata, and placenta accreta.

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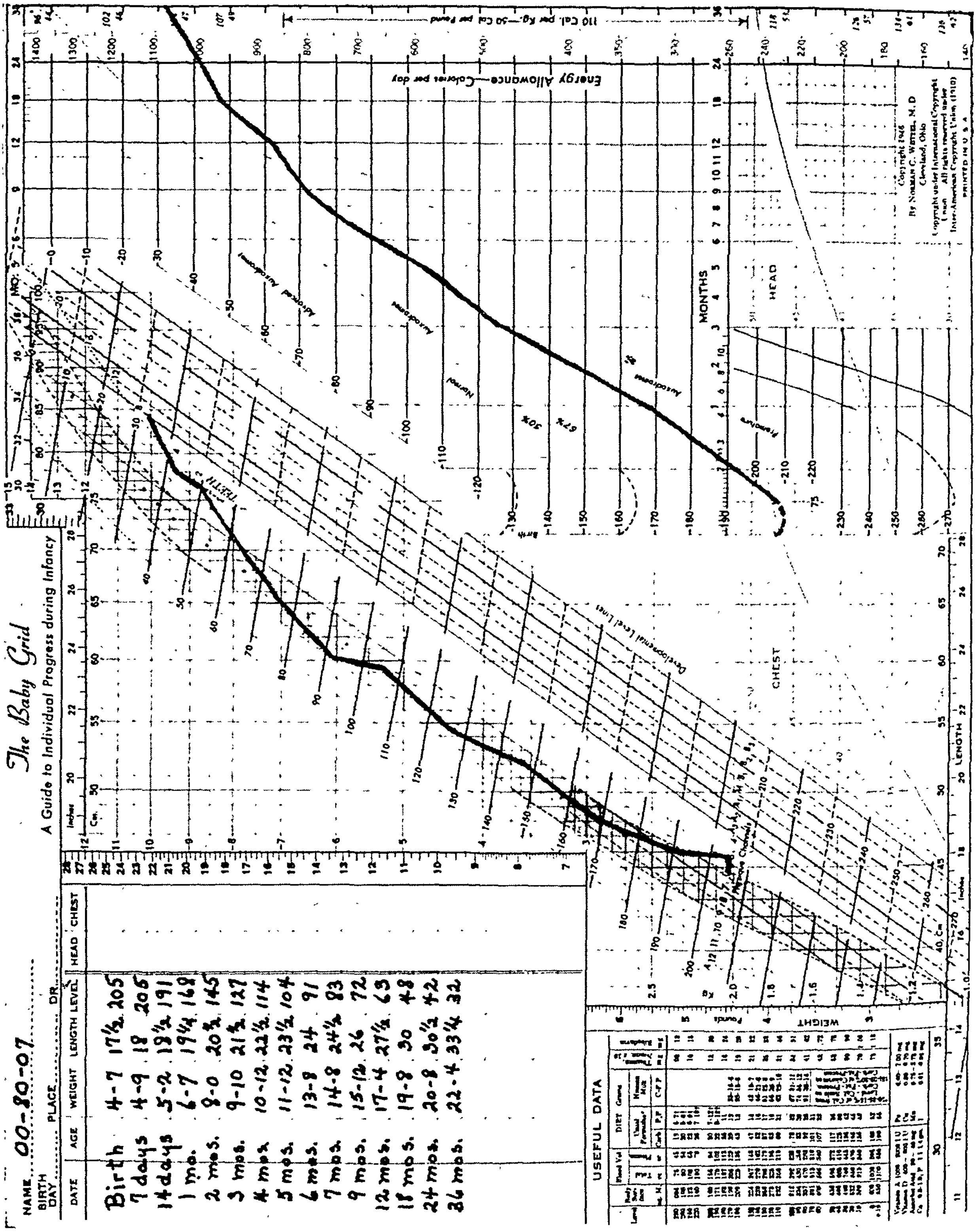

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BIRTH DAY

DATE	AGE	WEIGHT	LENGTH	LEVEL	HEAD	CHEST
Birth		4-7	17½	205		
7 days		4-9	18	206		
14 days		5-2	18½	191		
1 mo.		6-7	19¾	168		
2 mos.		8-0	20¾	145		
3 mos.		9-10	21½	127		
4 mos.		10-12	22½	114		
5 mos.		11-12	23½	104		
6 mos.		13-8	24	91		
7 mos.		14-8	24½	83		
9 mos.		15-12	26	72		
12 mos.		17-4	27½	63		
18 mos.		19-8	30	48		
24 mos.		20-8	30½	42		
36 mos.		22-4	33¼	32		

Fig. 1.—Brief period of neonatal adjustment, followed by continuous falling off in growth through two auxodromes by second year, *is shown here. This phenomenon was seen in 8 other premature infants of 18 in study group* whose progress was followed two years. Permission was granted by Dr. N. C. Wetzel and the National Education Association, Inc., for reproduction of the Baby Grid.

Some of the infants born with these unusual placentas had smaller measurements than their gestational ages would indicate. Figure 1 shows the growth curve of an infant born at 37 weeks' gestation weighing 1,446 Gm. (3 lb. 3 oz.). This infant, like 8 others of the 18 premature infants whose measurements were taken up to or beyond one year, adjusted rapidly to extrauterine life and began to grow immediately, without the prolonged and severe adjustment period characteristic of the usual premature infant. Figure 1 also portrays apparently permanent smallness in the size of this infant, like those of the other 8.

Table 1.—*Correlation Coefficients of Vital Measurements of Infants in Study*

	Female				Male			
	Study		Control		Study		Control	
Age, Mo.	r	P	r	P	r	P	r	P
Weight								
0-6	0.11	>0.1	0.57	<0.001	0.41	<0.02	0.30	<0.1
0-12	0.12	...	0.51	<0.01	0.21	>0.1	0.36	<0.05
6-12	0.84	<0.001	0.84	<0.001	0.76	<0.001	0.88	<0.001
Height								
0-6	0.61	<0.02	0.75	<0.001	0.56	<0.001	0.68	<0.001
0-12	0.36	>0.1	0.55	<0.01	0.32	<0.1	0.45	<0.01
6-12	0.67	<0.01	0.66	<0.001	0.72	<0.001	0.85	<0.001

Term Infants.—The infants whose growth is reported here were selected under the following conditions: (1) birth weight and length are known; (2) 6-month and 1-year weights and heights are known; (3) the child's general health and development are known; (4) only Caucasoid infants are reported in the growth data, because of insufficient numbers of Negroid infants satisfying the first three criteria; (5) infants with major anomalies are excluded from the growth data; (6) premature infants are excluded from the growth data; and (7) all remaining infants were divided according to sex and assigned to a study or a control group according to the description of the placenta. All infants are reported. These data are plotted on growth charts constructed from Stuart's and Stevenson's data.[6A] The placentas of infants in the study group had calcifications, white and red infarcts, fibrinoid degeneration, loss of large crescents of the edges, degenerating cotyledons, and old and recent abruptions.

In figure 2, *top,* are individually plotted data for growth in weight, height, and head circumference of male Caucasoid infants, divided into study and control groups. The data on the control infants remain, to a remarkable extent, within the percentile classifications assigned at birth throughout the first year. The data on the study infants show a marked ascending trend for the first 3 to 5 months for weight and for 6 months for height. The measurements of head circumference make no striking deviations. After completion of the ascent to higher percentile groups, the individual curves of the study infants conform to the movement of the percentile channels.

In figure 3 the means of the groups of male and female study and control infants are compared. Statistically, the significance of the difference between the means for weight is negative at birth but significant at the 2 to 5% level by the age of 6 months and maintains a similar relationship at 1 year. In tables 1 and 2 the correlation coefficients and the analysis of their significance reveal that the one-year heights and weights of infants in the control groups are predictable from birth measurements at the 1% level but that the one-year heights and weights of infants in the study group cannot be predicted at birth.

Comment

Placental Aspects.—The 40% incidence of observed placental variation in our series is lower than Williams'[3] observation of a 63% incidence in 500 consecutive deliveries. Our lower incidence may be due, in some instances, to failure to record adequate placental description and, in others, to the crudity of examination of unfixed fresh placentas. Placental variations, either unknown because of failure to be noted or of a degree insufficient to be noted, may have been present in the control group of infants studied.

As a matter of practical importance, no sure means are available to predict placental variation. The physiological reserves of this organ of transport for the fetus are apparently ample to meet its functions, unless structural change is extensive and severe. Adequate function may continue even with accumulation of many scars. Grosser[7] has pointed out in a study of comparative placentation that nature, by an evolutionary process, has encumbered the human placenta as well as endowed it with reserve capacity. The stage has been set for degeneration and a degree of tolerance to it. Current information does not allow clear-cut definition of normal variations in structure of the human placenta. Although several investigators have related placental dysfunction to fetal problems, the possibility remains that both might be due to the same

Table 2.—*Significance of Differences Between Means of Study and Control Groups*

	Means, Female				Means, Male			
Age	Study (n=14)	Control (n=30)	t	P	Study (n=14)	Control (n=30)	t	P
Weight								
Birth	7.43	7.13	1.18	>0.2	7.14	7.64	1.92	...
6 Mo.	17.66	16.59	2.39	<0.05	18.31	17.05	2.73	<0.02
12 Mo.	23.02	21.67	2.38	<0.05	23.43	22.04	3.36	<0.01
Height*								
Birth	19.6	19.8	0.66	...	19.5	19.9	1.25	...
6 Mo.	26.3	26.2	0.73	>0.2	26.9	26.5	1.96	<0.1
12 Mo.	29.7	29.6	0.66	>0.2	30.4	29.9	2.38	<0.05

* Lack of significance here accounted for by crossing of height values. See table 1 and figure 3.

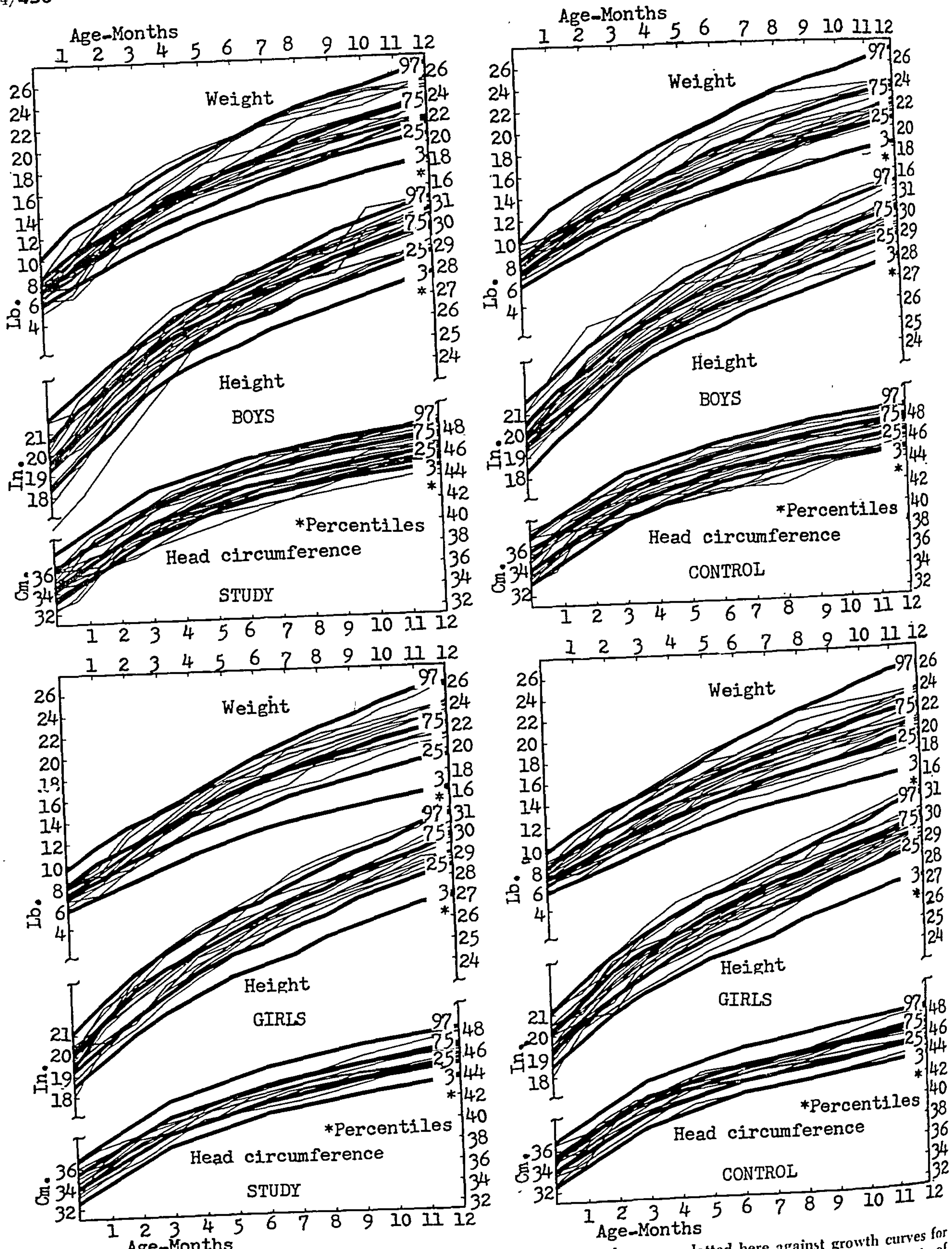

Fig. 2.—*Top,* individual growth measurements of boys of study and control groups, plotted here against growth curves for weight, height, and head circumference from data of Stuart and Stevenson.[6A] *Bottom,* individual growth measurements of girls of study and control groups. Curves of study infants have marked ascending trend for 3 to 5 months for weight and for 6 months for height and then remain within attained percentile channels. Curves of control infants remain within percentile groups assigned at birth. Head circumferences of both groups have no remarkable deviations.

factor and might not have a true cause and effect relationship. Studies to clarify these questions are sorely needed, for the circumstantial evidence pointing toward rewarding information in this area is strong.

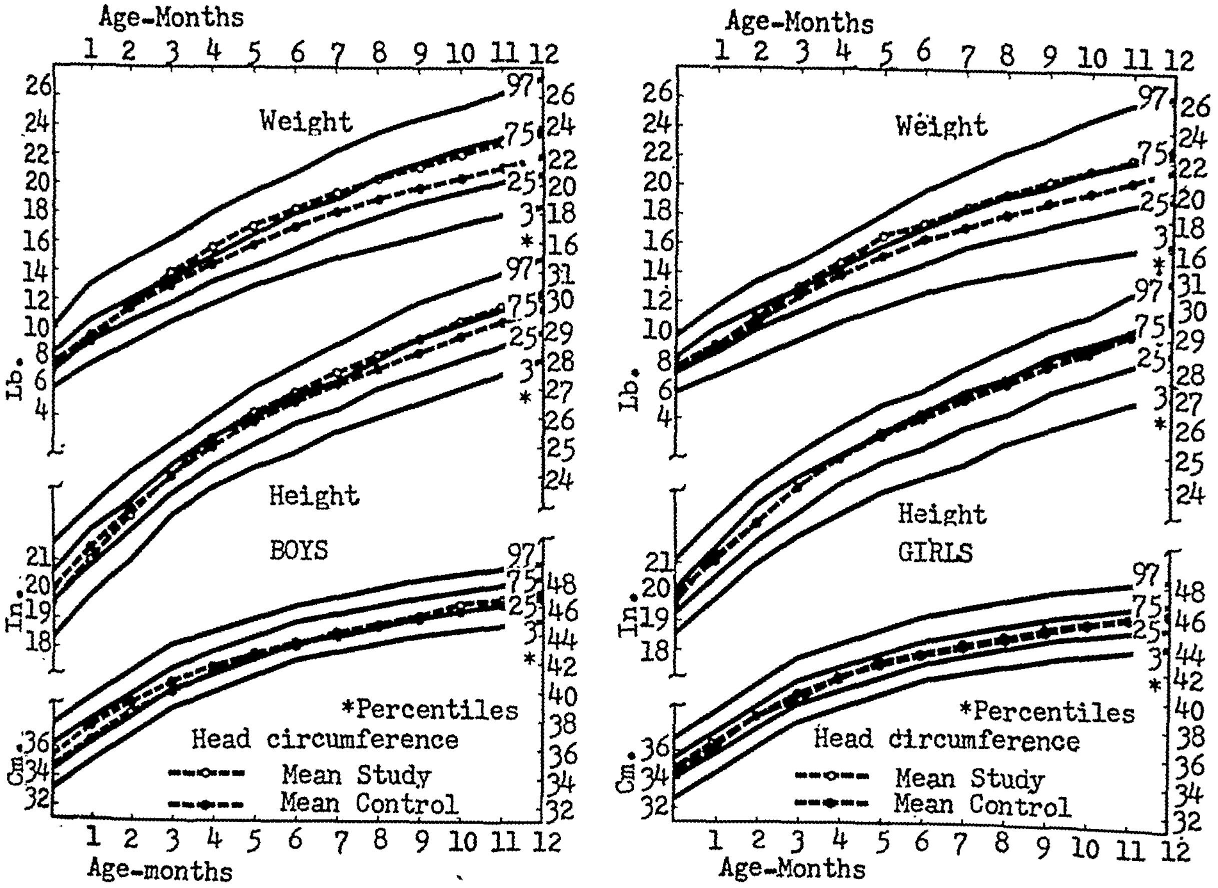

Fig. 3.—Mean values for study and control boys and girls. Statistical significance of differences between two means for weight is negative at birth but at 2 to 5% level by 6 months in both girls and boys.

Growth Aspects.—Minor disturbances of placental function might be expected to be reflected in growth disturbances in the same way as are nutritional deficiencies. These growth disturbances would be of major or minor degrees, according to the duration and severity of the defect. Again, it is of interest to note the apparently permanent smallness in size of some infants born with the physical measurements of prematurity. Furthermore, the infants born at term with term measurements grow as if recovering from a brief period of undernutrition, like that seen in infants recovering from acute infections or other temporary disturbances of metabolism. These apparent nutritional deficits at birth have been described by several authors,[1] both in stillbirths and in infants with the "placental dysfunction" syndrome, in cases in which placental defects have been seen.

Several students of growth[8] have remarked on the unpredictability of later height or weight from birth measurements. The indexes of correlations of growth in height and weight of the study and control groups suggest that placental variations may be a factor in prenatal deviations of growth from the genetically determined pattern.

Clinical Aspects.—Clinically, the study infants behaved as if starved, commonly had "colic," and frequently were not willing to discontinue their night feedings until three to six weeks later than control infants.[1a] Regurgitation, loose stools, and unfavorable reaction to early introduction of foods other than milk were noted frequently in the study infants' charts.

Nutritional Aspects.—Observations of the clinical behavior and growth phenomena of the study infants suggested that the nutritional aspects of these infants be examined (table 3). Since infants of the study group outgained those of the control group by 810 Gm. and their control fellows of equal birth weight by 1,350 Gm. in the first 6 months, a difference in nutritional needs is evident.

The differences in the average daily nitrogen retentions required to achieve these increments are presented by arithmetic subtraction.[9] Infants in the study group compared with infants of the same birth weight required daily retention of 178 mg. more nitrogen. Infants of the study group compared with all infants of the control group required daily retention of 107 mg. more nitrogen.

The amount of ingested protein from human milk which is retained in term infants ranges from 14 to 50% and averages 33%.[10] With use of this average, infants of the study group compared with infants of the same birth weight required daily ingestion of 3.3 Gm. more protein. Infants of the study group compared with all infants of the control group required daily ingestion of 2.0 Gm. more protein.

Investigative Aspects.—The variability of nitrogen retention reported in early infancy, even in the same laboratory and by the same investigators,[9] may be related in some instances to the observed growth phenomena of the study groups of infants. The statistical relationships between the growth phenomena observed and the placental variations seen may suggest that the two observations are related. Avidity for nitrogen and increased retention after acute or subacute prenatal depletion may have more importance than has been allowed, either in this presentation or elsewhere, with respect to both actual retention and efficiency of utilization of ingested protein.

TABLE 3.—*Additional Requirements Based on Arithmetical Differences Between the Groups*

	Weight Gained (14.8%P),[9] Gm.	Additional Nitrogen Retention Day (P=N×6.25), Mg.	Additional Protein Ingestion, Day (⅓ P Absorbed),[10] Gm.
Study group minus control group	810	107	2.0
Study group minus Stuart's[6A] equivalent ...	1,350	178	3.3

Conclusions

Forty per cent of placentas in 654 deliveries had gross variations at routine examination in the delivery room. A statistically significant relationship between placental variations and peculiarities of postnatal growth was seen. Gross examination of the placenta may be a useful clinical tool to forewarn the physician of some common problems of the first six months. This report is the result of intensive study of a small number of patients. No final conclusions can be stated, save that the relationship of the placenta and the fetus merits further study.

Greene and Redwood Streets (1) (Dr. Hepner).

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RELATION OF IMPAIRMENTS OF HEARING TO LONGEVITY.—Marked impairments of hearing or deafness apparently do not adversely affect mortality. In a long-term follow-up study of persons with such defects found upon examination for life insurance, the mortality experienced was no higher than that for persons insured at standard premium rates. This may reflect, in part, the fact that people with such impairments probably live more sheltered lives than the average person. Only in cases involving mutism was the mortality increased, being nearly 1½ times as high as the average for standard risks.—Hearing Impairment is Common, *Statistical Bulletin,* October, 1959.

THE NEWBORN INFANT

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In order to achieve further reductions of mortality in newborn infants it will be necessary to observe four principles. Mothers and infants must be followed for infections developing after discharge from the hospital, bacterial cultures must be made from infants or adults who may be acting as carriers, specific bacteriological study must be made on individual cases rather than periodic mass cultures of hospital personnel, and nurseries must be kept up to recognized standards. Among the problems awaiting solution are the cause and cure of the hyaline membrane syndrome, the improvement of criteria for selecting infants likely to require exchange transfusions in cases of hyperbilirubinemia, and the elimination of iatrogenic disease by more diligent precautions against the side-effects of drugs. Application of routine measures to entire nursery populations must not be substituted for attention to the individual newborn infant.

Infant mortality across the nation, which had fallen each year from 1952 through 1956, when it reached 26.0 per 1,000, rose in 1957 from 26.0 to 26.4; in 1958 it rose again to 26.9. For 1957 a part of the increased infant mortality was neonatal mortality. For 1958 the breakdown is not yet available. It appears that there are problems of the newborn infant which are not being met.

Many—perhaps most—of us have seen in our state and local hospital statistics a disappointing tendency for neonatal mortality to show either no fall or—more alarmingly—an actual rise. Intensive study of local situations may give more useful clues to what is wrong than can be obtained from the slower accumulation of national statistics. At least everyone can work on his own problems more rapidly and effectively than on those of the nation, and only by attention to the local and particular can we affect the national and general.

Infections

Staphylococcic Infections.—I do not know whether the national upswing in infant mortality is caused largely by nursery infections, but I do know that such infections are a major and increasing problem in many localities. The most common and troublesome ones appear to be staphylococcic infections acquired after—or, rarely, during—birth, usually not from the mother but from someone else, who not only carries but also "spreads" the organism. Often the spreader is another infant. With today's short-term stay of newborn infants in maternity hospitals, neither the infecting nor the infected infant may be recognized, and such hospital-acquired infections break out at home after discharge more common'y than while the infant is in the nursery. The organism which causes them is resistant to many antimicrobials but seldom resistant to all.

From these facts, principles of prevention and treatment—more fully and authoritatively published elsewhere by others [1]—emerge. We must (1) follow the progress of all infants after discharge; (2) make cultures in all cases when there are lesions in infants or adults, or when there is suspicion of "spreader" status in either—this may have to be done either after discharge or in the hospital; (3) make specific bacteriological diagnoses, with typing and drug sensitivity studies done on the few rather than mass cultures or "prophylactic chemotherapy" on total groups; and (4) in Wheeler's [1] words, "Keep a clean house and see that our nurseries meet the standards published by the American Academy of Pediatrics."

These are the main general principles. They may need many adaptations to fit specific epidemics and locations, but the uselessness of depending on mass cultures at regularly repeated intervals, or on routine prophylactic chemotherapy, must probably be universally accepted.

Other Infections.—This is not the only infection problem. The one encountered in premature infants in the Boston Lying-in Hospital is from bacterial infection, usually with Escherichia coli from the mother (occasionally with what seems to be a virus), which begins by producing an amnionitis or chorioamnionitis before the birth of a premature infant. Such processes—sometimes but not always occurring with early rupture of membranes—infect the fetus through the swallowed or inhaled amniotic fluid. However the infection gets across the mem-

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branes, it may often be the cause of the premature labor itself, for such amnionitis is distinctly less common in full-term infants. It tends to occur especially in the 1-lb. and 2-lb. (0.5-kg. and 0.9-kg.) premature infants rather than in the larger, more mature ones. The resultant intrauterine infections of infants are not usually epidemiologic nursery problems, but they interest us greatly in the possibility of early identification, treatment through the mother before birth, and the use of cord sections and amniotic fluid cultures for the pathological and bacteriological diagnosis necessary to useful action.[2]

These are only two of the several problems of neonatal infection, but in many parts of the country they are the most significant two. Only your own investigation of your local situation will tell you what specific infection problems you may have there or assure you that you have none.

Other Causes

The problem of infection has been taken up first among causes of neonatal mortality, because it should be capable of solution with present knowledge. However, in the mortality statistics of my hospital, at least, the hyaline membrane syndrome is a greater problem than that of infection. Although the solution to the hyaline membrane syndrome problem may already be staring us in the face among the various items of old and new information now available, we have not been keen enough to recognize it. I will, therefore, merely acknowledge the primacy of this problem [3] and pass on to matters which, although of less significance for neonatal mortality, offer more hopeful possibilities for action.

I shall mention two of these. One is the current and well-justified excitement over the newer knowledge of bilirubin.[4] Unfortunately, there appears to be no safer or better method of reducing hyperbilirubinemia than by replacement transfusion, and there is no means of knowing which 8 of any 10 individual infants with serum bilirubin concentrations of 20.5 mg. % might escape undamaged. At the present state of knowledge, most of the 10 will therefore have to have exchange transfusions unnecessarily. This does not, however, require the uncritical subjection of infants with lower bilirubin levels to this potentially dangerous procedure, and it does mean a serious burden of responsibility for anyone to whom we entrust an infant for replacement transfusion. Such a physician must be able to do this carefully and with reasonable safety.

Last, the consideration of bilirubinemia is a good place to insist on the most diligent precautions against side-effects of drugs and procedures which may be safe in older patients but are not so in newborn and premature infants. Administration of synthetic vitamin K can elevate bilirubin levels.[5] Sulfisoxazole (Gantrisin) can cause kernicterus when it is given in combination with penicillin.[6] Beside these two forms of iatrogenic disease related to bilirubinemia, it is to be hoped that none of us will forget the potential danger of administering an excess of oxygen to premature infants [7] or the unfortunate consequences of attempted mass protection by antibiotics. Recently it has been shown that chloramphenicol has a special toxicity when it is given to newborn mammals, including man.[8] It is a chastening thought that we might even now be making use (without absolute indications) of some nursery procedures which have unfortunate effects as yet unrecognized.

At the least, it seems justifiable to conclude that we must know what happens to our newborn infants (and not just in the first week or month but even in their school years); that we should keep them, what or who comes near them, and what goes into them clean and free from risk of carrying infection; and, finally, that we must give up our former idea that by supplying all requirements in large quantities to all babies—oxygen, vitamins, antibiotics, antihemorrhagic substances, and even routine x-ray examinations—we can protect the whole group and forget the individual patient. In fact, it is now sadly apparent that newborn infants, who have never previously been so mass-produced as now, must now be more than ever individualized.

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A NEW LOOK AT PREVENTIVE MEDICINE IN AMERICAN INDUSTRY

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Medical thinking and practice must be adapted constantly to changing social requirements. Since industrial operations and materials are changing continually and often radically, there is no hope of a permanent solution to the resulting problems. To match the trend toward a better brand of clinical medicine in industry, there must be a broadening and deepening of the physiological scope of the experimental work of the laboratories devoted to occupational medicine. A proper share of the educational facilities of the United States should be used for courses of instruction for physicians in industry, and the necessary means for investigative work should be apportioned to productive research in occupational medicine.

Medicine in American industry has acquired a greatly improved status in recent years and one which holds great promise, not only for its own future development but also for the fulfillment of the growing responsibilities of medicine generally, within a society that has surrounded itself with a multitude of new and artificial dangers to life and health in its headlong technological pursuits. It would not be feasible, in the time available, to describe the dangers that lurk in the work places of the nation, much less those that have wider distribution in the community as a whole. Neither would it be fitting or truthful to claim that the improved status of the physician in industry derives entirely from his detailed knowledge of the nature and consequences of human exposure to these dangers or from his ability to recognize or counteract them. Rather, we must face the fact, however chastening it may be, that while physicians in industry are much more aware than are others of the potentialities for harm that lie in the impact of technology and industry on man, individually and collectively, we have not learned enough to interpret these potentialities with completeness or precision, nor have we been able to establish sound criteria for human safety and health, on even the pragmatic basis of freedom from obvious injury or disease, in more than a few of the many situations that now present themselves.

What we have done, in comparatively recent years, is to obtain possession and, to some degree, mastery of the tools of research; to gain access, or at least to reach the threshold of access, to the facilities of medical and hygienic education; and to establish the right of the physician in industry to share, equally with his colleagues in other specialized fields of medicine, in the duties and privileges of the organized profession. In short, what we have achieved is opportunity and, with it, responsibility. Let me dwell, for a moment, on the three features of our newly acquired position, as barely mentioned above.

Research in Occupational Medicine

Occupational medicine has grown out of its swaddling clothes and is reaching out into more extensive and, at the same time, more difficult fields of investigation. This is not to say that highly productive and mature contributions have not come out of research in this field in the past. It is rather to point out, perhaps wishfully, that a present trend toward more fundamental approaches to basic problems is discernible in the general body of research in occupational (and general environmental) medicine. For some time, much of the investigation in industrial health has been concerned with the elementary observations and procedures of industrial toxicology and with the determination, within the laboratory, of tolerable concentrations of dangerous substances in the atmosphere of work places. Such work has been and still is required, and it would be both false and pretentious to look on it with disdain. In fact, the work horse of industrial hygiene has been the industrial toxicologist, who has not always or even usually been a physician; the special flavor of the accomplishments in industrial hygiene, in the United States, has come from the teamwork of the industrial toxicologist and the environmental engineer. The maintenance of good health in present-day industry, however, demands something more than the specification of barely tolerable levels of stress and the applications of environmental engineering tailored to such specifications. There is need for better criteria of human health and safety than can be found in descriptive environmental standards related to obviously injurious forms of stress. This need can be fulfilled only by a new and expanded type of industrial toxicology, namely, experimental medicine in the broad sense, in combination with a much

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more highly developed program of medical supervision in industry, based on precise clinical and epidemiologic interpretations of the physiological responses of workmen to environmental conditions.

Colleagues in the field of environmental control have viewed the physician in industry somewhat skeptically or even critically, in many instances with good reason. If the best we can do is to recognize disease or injury after it is apparent to intelligent laymen, our skill is not sufficient to our task. Moreover, if the prevention of disease depends solely on environmental control, and if the criteria of need thereof reside in the technical examination of the environment, our contribution to industrial hygiene is negligible. But our skill need not be so circumscribed nor our contribution so meager. By adaptation of research to the needs of clinical medicine, by extension of such research into the work situation, and by inclusion of the industrial physician in the investigative team, experimental medicine will become the basic element in medicine in industry, and the leadership of the industrial physician in the practice of industrial hygiene will become the vital force in industrial health.

This means, of course, that the chief goals of industrial medical research are the elucidation of physiological mechanisms and the development of useful clinical and statistical procedures for the recognition of such mechanisms in action. It means also that the practice of medicine in industry will be transformed, from being concerned primarily with the diagnosis and therapy of occupational injury and disease, into a productive function of disease prevention and health maintenance. That this transformation has not been made, generally or even widely, is evident, but there is a trend in that direction which is revealed by a broadening of the base and a deepening of the physiological scope of the experimental work of the laboratories and, even more importantly, by the appearance in industry of a better brand of clinical medicine, in which have been incorporated clinical toxicology and the disciplines of epidemiology and biostatistics. Medicine in industry, as indicated by its affiliation with the American Board of Preventive Medicine, is coming to be preventive medicine—a somewhat different brand of preventive medicine than has been known previously, but nonetheless preventive medicine as it should be and may become more generally.

Education in Occupational Medicine

Whether formal graduate education in occupational medicine came into existence in response to the changed and changing concept of research and practice in the field, or whether the newer concept was born of the educational program is not, and need not be, clear. It seems likely that both of these developments originated in response to much the same stimuli and that each has influenced the other during the period of their association. The two are now inseparable, however, and it is impossible to foresee a time when they will not be. This fact is not appreciated as fully as it should be, and, at the risk of overemphasizing the obvious, I am constrained to call attention to the utter dependence of the practitioner of medicine in industry on precise knowledge of the qualitative and quantitative relationships and interactions of the persons for whose health he is responsible and the artificial factors introduced into the work environment in consequence of the day's work. If the work environment were to remain constant, or if the working population were to remain unchanged, the hygienic problems might be solved once and for all, but since industrial operations and materials are changing constantly and often radically, and since the persons at risk are changing individually and collectively, there is no hope of a permanent solution. An established and unvarying program of industrial hygiene, therefore, is more likely to be an expression of professional sterility than of any other quality of the professional mind.

The point to these remarks, in relation to the education of the specialist in occupational medicine, is that the physician in training must be brought up in the environment of occupational medical research. Certainly, he must become familiar with the disciplines of preventive medicine generally, and he must develop an understanding of the nature and effects of the many harmful materials and forms of energy that are dealt with in industry, but he must also recognize the necessity for inquiry, the feasibility of using his powers and instruments of observation and of summoning the aid of other trained technical observers of the industrial environment, toward the end of understanding.

The spirit of inquiry is a state of mind, just as its opposite is the acceptance of the status quo and the authority of the word, especially the written word. Thus, in the educational institution in which the investigative attitude is strong, yet not divorced from teaching, graduate training is an absorbing and dynamic experience for both instructor and graduate student. If this atmosphere can be maintained alive and thriving, the educational process will not become sterile and, above all, will not become a mere structure of courses and of timid compliance with formal requirements.

In these days, when educational qualifications tend to be established by agencies outside the institutions of learning, it behooves the latter to look to their responsibilities. It is well for professional organizations to prescribe minimum standards for the training and performance of their members. But it is not well—it is fraught with the evils of authoritarianism and of mediocrity—for educational institutions to adopt, or be coerced into the acceptance of, the requirements of external agencies as their criteria for the quality of their educational program. The universities and other educational institutions of the country are indeed the refuge and, in some degree, the source of the free minds of our men and women, the main sources of our knowledge and cultivation, and the mainstays of our civilization. If they are not, they have defaulted in their responsibilities and have failed miserably in their primary function. They should lead the intellectual life of the United States, including its professional life, and we should turn to them for leadership, lest they fail, through lack of demand, to fulfill their proper role in our society. I do not believe they have failed or are likely to fail. Despite the criticisms that are leveled at American education in our time, and despite the tremendous demands that are being made on them now and are soon to be multiplied, our institutions of advanced learning have established and maintained high standards of achievement, and their product in men and ideas is generally of high quality.

There are now seven universities that offer graduate training in occupational medicine and industrial hygiene, and several others are taking steps in that direction. About 40 graduate fellows in occupational medicine alone can be accommodated annually in these schools. Each of these schools, and one or two others, is giving postgraduate courses of instruction for physicians in industry. The efforts in this direction could and would be amplified if there were a greater demand for them on the part of physicians.

In the field of undergraduate education in medicine and engineering there is, at present, a serious lack of familiarity with and attention to the problems of industry and of our complex industrial society. This is a fault which must be remedied in the near future, if the professions concerned are to meet the hygienic needs of our time. It is not to be expected, nor is it desirable, that training in any way equivalent to that of the specialist in occupational medicine and environmental hygiene should be provided in the undergraduate years of medical and engineering study. It is essential, however, that every graduate in medicine and engineering should have some grasp of the impact of technology on our society, some realization of the methods of professional investigation and practice in these fields of action, and some appreciation of the opportunities afforded therein for specialized professional service. It is my considered opinion that this will not and cannot be done with appropriate skill and balance until sound facilities for research and graduate instruction in these specialized fields have been developed and have become a recognized part of the armamentarium of a large proportion of the university centers of education in medicine and sanitary engineering in this country. Only through the eyes and on the basis of the experience of persons with a wide range of professional knowledge and technological competence can problems and their handling be visualized in the course of regular basic training of physicians and engineers.

Occupational Medicine as a Specialty

It is generally known in medical circles that occupational medicine and the related practice of aviation medicine have gained recognition as medical specialties by affiliation with the American Board of Preventive Medicine. This was not accomplished without much soul-searching and anguish, for the desire was strong among the physicians in industry for an independent board, and the official pressure exerted to fit various and somewhat disparate elements of what had long been known, without definition, as industrial medicine, into a well-defined pattern was resisted strenuously. The true significance of this travail lay not in the travail itself, as any experienced accoucheur could have foretold, but in its offspring. For this union with preventive medicine has brought forth, true to its lineage, preventive medicine in industry, more accurately called occupational medicine, with a clear title to the disciplinary resources alike of preventive medicine, clinical medicine in industry, and the medical aspects of environmental hygiene. Out of the struggle, the heritage, the products of research, and the educational regimen has emerged a lusty adolescent, which gives promise of growing to the full stature of a responsible and effective member of the family of medical specialties. And now the test of its maturity lies ahead of it, and the task of salvaging the health and stamina of a highly industrialized society, jeopardized by its technological cleverness and its reckless quest for power, looms large on its horizon. This task cannot be accomplished by the specialists in occupational medicine alone, however skillful and dedicated they may be, nor can it be achieved by all of the medical and hygienic resources of the United States, unless they are alerted to the threat and oriented in greater measure to meet it. It may be, however, that preventive medicine, in making occupational medicine its own, and in moving into the broader field of medical practice, generally, will find a new armamentarium with which to combat the man-made hazards of modern life as effectively as it has many of the natural threats of pestilence and epidemic disease.

Comment

As was said early in this forward look at preventive medicine in industry, what we have now achieved is opportunity. We in occupational medicine have the advantage of growing toward professional maturity at a time when great skill is being employed and rapid progress is being made in many fields of medical research; when, despite the heavy demand for and the relative dearth of trained investigators, the scientific resources of the United

States are extensive and of high quality. We can obtain our share of these resources. At this time, also, the educational facilities of the country, in our general field, while under great and increasing pressure, have been developed to a high level of quantity and quality.

This is also a time of stress in the practice of medicine, when ideas and relationships are under examination, and when there is urgent need for appropriate adaptations of medical thought and practice to social requirements. We have come on the scene at a propitious time. While congratulating ourselves on our newly acquired status, let us take sober thought for our new responsibilities for promoting and carrying out productive research; for further cultivating educational discipline by which to train technically skilled and socially adept practitioners of our science and art; and for establishing modes and forms of medical procedure in keeping with the needs of our people.

PHYSIOLOGY OF THE MYOCARDIUM

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By catheterizing the coronary sinus it is possible to make chemical comparisons of the venous with the arterial blood in the coronary vessels of the human heart in situ. Metabolic studies by this technique have demonstrated the importance of fatty acids in the nutrition of the myocardium. By the introduction of microelectrodes into the interior of single cells from the myocardium, the atrioventricular node, and the ventricular conducting system it is possible to follow electric changes and ionic fluxes in small units. This method has thrown new light on the significance of potassium and oxygen and the mechanism of fibrillation and pulsus alternans. Comparable advances have been made in the chemistry of myocardial proteins, the basic pharmacology of the heart, the pathological physiology of ischemia and anoxia, and the metabolism of the myocardium in congestive failure or after infarction.

Within the last decade, investigators interested in the heart have begun to study this organ from a molecular level. Anatomists are now investigating the submicroscopic morphology of the heart, while physiologists and clinical investigators, no more content to measure pressures and flows, have begun to explore the electric activity of single heart muscle cells and are studying the metabolism of the heart; together with biophysicists they are investigating the structure and function of the contractile proteins of the normal and the diseased heart. With the help of pharmacologists, they are exploring the action of digitalis on the cell membrane and on the contractile proteins. Recent experiments have pointed to the importance of the organizational relationship between catecholamines and the myocardium.[1] Out of this has come a different approach to heart disease and its treatment, both medical and surgical. It is the object of this report to review some of these newer aspects of the physiology of the myocardium and to relate them, whenever possible, to diseases of the heart.

Nutrition of the Heart

The advent of catheterization of the coronary sinus has made it possible to study the use of various substrates by the human heart in situ and to observe the myocardial extraction of substrates and oxygen. The human heart uses considerable amounts of fatty acids in addition to glucose, pyruvate, lactate, amino acids, and ketones.[2] When the fatty acid level in blood is increased by a high fat intake, the contribution of fatty acids to the total oxygen usage of the heart is frequently above 100%.[2] It is likely that this increase in the apparent usage of fatty acids by the heart represents storage of fat in heart muscle. Fatty acids exist in plasma both as nonesterified (free) and esterified fatty acids. Free fatty acids are present as anions; as the name implies, the carboxyl group of these acids exists in the undissociated state and is not involved in the formation of an ester bond. Fatty acid anions do not exist free in plasma, however; they are bound to al-

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bumin and each albumin molecule bears two sites with high affinity for fatty acids.[3] Erythrocytes also bind fatty acids, and this binding is interpreted in terms of the presence in the cells of a large number of binding sites. It could be shown in the laboratory that, as the concentration of free fatty acids in blood increases, their binding to the red blood cell increases disproportionately so that at high, unphysiological concentrations of fatty acids most of them are bound to the red blood cells.

The main source of the nonesterified fatty acids is in the adipose tissue and they disappear rapidly from the blood; their main function appears to be the transport of fatty acids from adipose tissues to the organs where they are used.[3] Thus, the quantity of fatty acid moved by this route should represent an important substrate for cellular oxidation and energy production. Indeed, as first demonstrated by Gordon and confirmed in our laboratory, free fatty acids represent an important energy source for heart muscle in the fasting state.[2] It has been found that the iodine number, representing the number of double bonds and therefore the degree of unsaturation in the fatty acid molecule, is higher in coronary sinus than in arterial blood. This points to a proportionately greater use of saturated fatty acids by the heart.

Heparin decreases the lactescence of plasma in vivo because of breakdown of chylomicrons; this is accomplished by the activity of an enzyme, the lipoprotein lipase, activated by heparin, which splits esterified fatty acids into the free form and into glycerol.[3] Although this action of heparin has been used in the treatment of atherosclerosis, nothing is known about the mechanism by which heparin causes lipoprotein lipase activity to appear in the blood; furthermore, the effect of heparin has not as yet been proved to be of definite value in the treatment of coronary heart disease. Work from our laboratory[4] has shown that the injection of heparin increases the concentration of nonesterified fatty acids in blood but does not elevate its myocardial usage. It has been claimed that a high degree of lactescence reduces the coronary blood flow in man and that the administration of heparin restores coronary blood flow to normal. This finding is of great clinical importance, but studies on dogs[4] have failed to demonstrate a similar effect. It appears from these investigations that fatty acids are of great importance in the nutrition of the heart muscle. No conclusions, however, are warranted at this time on the possible connection between these findings and on the relationship of lipids to coronary atherosclerosis.

Electric Activity of the Heart Muscle Cell

It has now become possible to record the electric activity of a single heart muscle cell by inserting a microelectrode with a tip of about 0.5μ into the interior of a cell. This permits recording of the potential difference across a limited area of muscle membrane. Thus, the time course of depolarization and repolarization of the heart muscle cell can be recorded and accurate measurements of a potential at rest (the resting potential) and during depolarization and repolarization (the membrane action potential) can be made. The transmembrane potential thus recorded from a single fiber of the spontaneously beating dog ventricle shows a constant resting potential during diastole, an abrupt phase of depolarization that terminates in a peaked reversal of membrane polarity, a plateau of long duration during which the membrane potential is close to zero, and a final phase of slow repolarization. Auricular transmembrane potentials are similar, but the plateau phase is missing.

Transmembrane potentials have also been recorded from the atrioventricular node and the ventricular conducting system. The ionic fluxes which determine those potentials and the changes of the resting and action potential under various conditions, such as anoxia and cardiac arrhythmias, are of particular interest. Studies on the intracellular potentials have helped us to understand the action of drugs used in the treatment of cardiac patients, particularly the cardiac glycosides, as well as the mechanism of some of the cardiac arrhythmias. The resting potential probably results from the difference in potassium concentration within and outside the heart muscle cell; the different phases of the action potential, on the other hand, are due to inward movement of sodium during the phase of depolarization, while repolarization may result from an outward flux of potassium. These processes are likely to be passive, but many studies suggest that the ionic "status quo" is reestablished between the periods of excitation by an active metabolic process of the cell membrane itself (the sodium-potassium pump). Thus, the production of action potentials and the propagation of electric stimuli appear to arise more from an increase in permeability that permits ions to move downward across their respective concentration gradients than from metabolic energy.

The recording of ventricular transmembrane potentials has helped us to understand the mechanism of electric alternation, ventricular tachycardia, and fibrillation.[5] Electric alternation could frequently be recorded from individual fibers before the onset of ventricular fibrillation. Mechanical alternation was always present when pulsus alternans was recorded. However, mechanical alternation did occur without demonstrable alternation in the single fiber electrode. It appeared likely that changes in the action potential were primary and that changes in mechanical contraction were secondary. Electric alternation, as recorded from several single cells simultaneously, was not observed in all cells of any preparation studied but was present in only one-third to two-thirds of the cells punctured in any single heart. Fibers showing alternation were not grouped but were scattered widely throughout the ventricle. Each fiber from which electric events were recorded showed action potentials with every beat. Therefore, it is unlikely that some myocardial cells take part in every second beat only and are refractory during the alternate cycle, a concept which has been widely held in various forms.[5] Rather, electric and mechanical alternation appear to be related to the behavior of individual fiber membranes and contractile elements.

The effect of oxygen lack has also been studied with the use of intracellular electrodes.[6] When this technique has been used on isolated, electrically stimulated anoxic rat atria, it has been shown that after the onset of anoxia the height of the action potential fell after four minutes of anoxia. However, contractility diminished within 1 to 2 minutes and progressed to complete cessation of activity 15 to 20 minutes later. The action potential shortened after a brief period of anoxia, but the membrane resting potential diminished only slightly. No action potentials were elicited after 17 minutes. In cat papillary muscle at low oxygen tensions the duration of the action potential shortened rapidly, followed by a diminution in the amplitude. In the dog's ventricle, cessation of coronary perfusion led to shortening of the action potential four minutes after interruption of the coronary circulation. The amplitude of the transmembrane resting potential fell to an average of 65% of the control value at the time of complete cessation of electric activity.[6] After 20 minutes of complete ischemia, all spontaneous mechanical and electric activity has ceased.

The findings are compatible with a more rapid passive transfer of potassium ions outwardly across its concentration gradient. The diminution of the amplitude of the transmembrane resting potential during anoxia could result from an increased uptake of sodium and consequent loss of potassium by the cell during recovery.[6] The fall in the amplitude of the action potential can be related to the effects of the lowered resting potential. It is also likely that the alterations induced by anoxia in the ionic transfer across the cell membrane are closely related to the high-energy phosphate concentration within the cell.

Helpful as these transmembrane potentials are in reaching an understanding of the changes in the excitability of the heart muscle, the final interpretation must wait until these potentials can be correlated with simultaneous and rapid measurements of ion fluxes across the cell. The use of the intracellular sodium and potassium electrodes may be necessary in achieving this goal.

Contractile Proteins of Heart Muscle

The discovery that the muscle proteins, actin and myosin, combine to form actomyosin complex, the contractile protein in muscle, has shed much light on the nature of the alterations occurring in contracting muscle at the molecular level. The muscle protein myosin itself has adenosine triphosphatase (ATPase) activity inhibited by magnesium and activated by calcium.[7] Actually, myosin itself can be split by proteolytic digestion into two components, only one of which is endowed with ATPase activity. This ATPase activity plays an important role in muscular contractions by breaking down adenosine triphosphate (ATP), a high energy phosphate compound, thus making the energy available for muscular contraction.

Actin is obtained from the muscle residue from which myosin and all the other soluble proteins have been extracted; a globular or G form is contained in aqueous extracts, but salts change this into the fibrous or F actin. Here too ATP is important since it is involved in the polymerization of actin and may be an important part of the actin molecule. One of the most striking properties of F actin is its ability to form a complex with myosin, leading to the formation of actomyosin; this compound has high viscosity and possesses a considerable degree of ATPase activity in the presence of magnesium. When ATP is added to actomyosin, striking physical changes, such as a drop in viscosity, occur. It is conceivable that the interaction between actin, myosin, actomyosin, and ATP and the various ions is responsible for the events taking place during contractions of skeletal and heart muscle. Szent-Gyorgyi's original observation that actomyosin threads contract on addition of ATP points strongly to the fact that actomyosin is indeed involved in contraction of the whole muscle. The role of ions in these events is particularly conspicuous; ions play a dominant role in the action of cardiac glycosides and will be discussed in a subsequent paragraph.

Fundamentally, actomyosin prepared from heart muscle behaves like the proteins prepared from skeletal muscle. However, the ATPase activity of cardiac myosin is one-third of that of skeletal muscle, and it is much more resistant to proteolytic enzymes.[7] Cardiac myosin requires a tenfold level of these enzymes to produce the same viscosity changes in skeletal muscle. This finding agrees with the observation made in our laboratory that the contractility of actomyosin prepared from human hearts obtained at autopsy remains unimpaired as late as six hours after the death of the patient.

It is of particular interest to the physician concerned with the molecular basis of heart disease that these contractile proteins of the heart can be studied in systems that stand halfway between the whole muscle and protein enzyme preparations. There exist several of these models; in one of them, ions, including potassium and sodium as well as ATP, have been removed by prolonged extraction of the muscle strips in water and glycerol. These glycerinated fiber models contract on addition of ATP. Another method for reconstructing a model of the contractile system consists in producing surface films of actomyosin solution which can be compressed into bands. With this method, one can record, without appreciable friction, shortening of the band at considerable magnification.

The appreciable resistance of actomyosin bands to proteolytic enzymes has already been mentioned. It has made possible a study of the contractility of actomyosin bands prepared from failing human hearts (to be discussed below); a significant diminution in contractility under these conditions has been demonstrated. It has also been shown that digitalis preparations fail to influence the contractility of these bands. Glycerinated heart muscle strips have been used to demonstrate the importance of a sufficient supply of ATP on contraction. Through these preparations, the cardiologist has learned that the contractile proteins of the heart may play an important role in the mechanism of heart disease and that factors influencing the contractility of actomyosin such as ionic strength and composition of ions may be of fundamental importance in the understanding of drugs which act on the heart.

Pharmacology of the Myocardium

Effects of Glycosides and Catecholamines.—Studies on the action of digitalis on the myocardium illustrate how the general aspects of nutrition of the heart, of the electric activity of the cell as dependent on ionic movements, and of the contractile proteins can be integrated. Catheterization of the coronary sinus has made it possible to study the effect of cardiac glycosides on the use of substrates and oxygen by the heart. It is now generally accepted that digitalis preparations have no effect on myocardial oxygen consumption. However, since they increase the work of the failing heart, they elevate myocardial efficiency. A study of the mechanism by which this is accomplished represents a real challenge.

Glycosides: The first question is concerned with the possible effect of the glycosides on the use of foodstuffs by the failing heart. After administration of lanatoside C (Cedilanid) no significant change in the respiratory quotient or the extraction of foodstuffs by the human heart in situ is noticed. This suggests that the improvement in work capacity of the failing heart induced by glycosides must be the result of the action on energy liberation or, more specifically, on the factors governing the contractile mechanism of the heart. However, when the glycoside digoxin is added to the bath surrounding an actomyosin band, the ATP-induced contractions are not different from those induced by ATP alone. Furthermore, digoxin does not change shortening of glycerinated skeletal muscle, and lanatoside C influences neither the speed nor the force of contraction in this preparation; digitalis does not reverse the decrease in contractility of cardiac actomyosin bands prepared from the heart of patients who died in congestive heart failure.

These negative results, however, do not exclude an effect of the glycoside preparations on the contractile proteins. They only demonstrate that something is missing under the artificial conditions existing in these model preparations. This missing link is, in all likelihood, the cell membrane and with it the effective concentration and distribution of ions in and outside the heart muscle cell. The importance of ions on the effect of cardiac glycosides can be indirectly ascertained by the recording of transmembrane potentials of a heart muscle cell. Digitoxin, for example, appears to shorten membrane action potential, particularly as a result of shortening the phase of repolarization.[8]

An effect of digitalis has also been noted on the electrolyte balance of the whole heart. Wood and Moe,[9] for example, using the heart-lung preparation, found good correlation between the magnitude of the efficiency increase of the heart and the rate of potassium mobilization from the heart muscle. However, the injection of lanatoside C into patients with and without heart failure failed to reveal any interference with the potassium or sodium balance of the human heart.[10] Recently it has been shown that the injection of acetylstrophanthidin resulted in increased concentrations of potassium in coronary vein blood. It is now considered likely that cardiac glycosides interfere with the metabolic or active phase of sodium and potassium transport. According to Szent-Gyorgyi, the diminution of potassium within the cell increases contractility through loss of "repellent" action which the positive charged potassium ions surrounding the myosin particles exert.

Catecholamines: The cardiac action of catecholamines is entirely different from that of glycosides. Aside from the absence of cumulative action, and the rapid onset and termination of their cardiac effect, their effect on the molecular level is quite different. For example, while digitalis in therapeutic doses fails to alter cardiac metabolism but does raise myocardial efficiency, norepinephrine and epinephrine lower myocardial efficiency by increasing myocardial oxygen consumption. Only in doses so small that these amines fail to exert a positive inotropic effect do they increase myocardial efficiency by lowering myocardial oxygen consumption.[11]

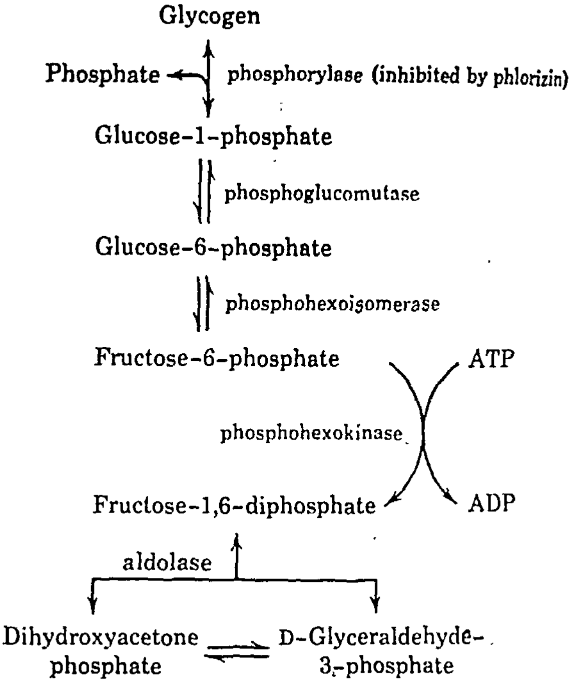
Although the amines do not exert a cumulative effect on the heart, norepinephrine can be stored in the heart muscle. After intravenous injection of the amino acid DOPA (dihydroxyphenylalanine), a precursor of norepinephrine, the concentration of norepinephrine in heart muscle is greatly increased.[1] Yet this stored amine exerts no pharmacological effect on the heart unless it is mobilized by reserpine, suprathreshold stimulation, or nicotine.[12] In addition, it now appears likely that the spontaneous failure of the heart in the heart-lung preparation results from a diminution in the total sum of catecholamines in the perfusion fluid. When liver and spleen are included in the perfusion circuit of a heart-lung preparation, the cardiac efficiency increases because of the small amounts of catecholamines secreted by these organs into the perfusion fluid, where they can exert their effect on the heart.

The Anoxic Heart Muscle

The problem of ischemia and anoxia has gained additional practical importance ever since the surgeon has begun to operate on the arrested nonperfused heart during cardiac bypass operations. For physiologists and clinicians this problem is not new; clinicians have been aware of the connection between "ossification" of the coronary arteries and angina pectoris since Jenner and Parry's publication in the middle of the 18th century. Chirac studied the effect of occlusion of the coronary arteries at the end of the 17th century, and Cohnheim published his classic studies on experimental occlusion of the coronary arteries in 1875. The question modern surgery has raised is not only what happens to heart muscle during anoxia but whether these changes are reversible if normal circulation to the myocardium is reestablished. In the heart, as in the rest of the body, death is not the end of all biological processes. Many biochemical reactions continue for a considerable period. Yet the ability of any organ to function as a whole depends on the resistance of its weakest link.

Some of the features of the effect of anoxia on the heart muscle have already been discussed. Changes in the configuration of transmembrane potentials occur four minutes after anoxia.[8] No transmembrane potentials can be elicited after 20 minutes of complete myocardial ischemia. In contrast, the contractile proteins of the heart appear extremely resistant to anoxia. An interval of from two to six hours between the death of the patient and the preparation of actomyosin does not affect the shortening of actomyosin bands prepared from human hearts obtained at autopsy. In contrast, processes concerned with energy production in the heart muscle are rapidly affected by anoxia. After one hour of anoxia the oxygen consumption of heart muscle slices was diminished to 40% of their control value.[13] The high-energy phosphate compound ATP shows the fastest disappearance rate.[13] The increase in inorganic phosphate, as observed under these conditions, is the result of breakdown of ATP and phosphocreatine. Glycogen also disappears rapidly from anoxic heart muscle as a result of considerable glycolytic activity.[13] In addition, nucleotides such as oxidized diphosphopyridine nucleotide (DPN) and reduced triphosphopyridine nucleotide (TPN) decrease with time. Of particular interest is the observation that the concentration of glucose-6-phosphate in anoxic heart muscle first increases and then decreases.

The elevation of hexose-6-phosphate after short periods of anoxia is, in all likelihood, due to the high rate of glycogenolysis which also occurs, as Cori [14] has shown, during anoxia and at high rates of stimulation of the muscle. Recent evidence from our laboratory has also shown that, while hexose-6-phosphate level increases under these conditions, the levels of fructose-1,6-phosphate and dihydroxyacetone phosphate in heart muscle diminish. This is in line with the observation that the rate of glycogenolysis occurs more rapidly above the level of the enzyme phosphohexokinase, which catalyzes the reaction fructose-6-phosphate to fructose-1,6-phosphate (see figure).[14]



Reperfusion of the heart with oxygenated blood after interruption of the coronary circulation for as little as 15 minutes does not, in many cases, diminish the rate of glycolysis, although slowing in the disappearance of ATP has been recorded. Furthermore, reperfusion of the heart leads to a diminution of the hexose-6-phosphate level; the diminution of this intermediary product of the glycolytic pathway could result from diffusion of this compound out of the anoxic heart muscle cell. This, however, is unlikely, since no glucose-6-phosphate could be recovered from the perfusion fluid. In addition, Cori and Cori [15] were unable to demonstrate diffusion of hexose-6-phosphate from anoxic frog muscle into the surrounding medium. It is probable that the diminution of glucose-6-phosphate results from increased activity of phosphofructokinase (see figure). Cori [14] has indicated that during anoxia due to partial disappearance of the functional boundaries within the cell, more substrate is made available to the enzyme; it has been shown that an excess of ATP leads to inhibition of purified fructokinase because of a high concentration of ATP relative to that of free magnesium. It is conceivable that lack of ATP, as it exists in anoxia, might result in increased activity of phosphofructokinase.

These findings demonstrate, therefore, the severe changes which follow complete interruption of the coronary circulation for even brief periods and stress the importance of maintaining adequate coronary perfusion.

The Myocardium in Heart Disease

Congestive Failure.—It is strange that one of the greatest mysteries in congestive failure has been the difficulty of finding any physiological or pathological changes in the heart muscle in this condition. It is true that in terms of pressure and flow physiological changes are easily discernible: the cardiac output is usually diminished, except in cases of high output failure, and incomplete emptying of the heart leads to increased initial length and tension in the cardiac ventricle, thence to increased pulmonary artery and peripheral venous pressures. But the question of why the "weakened" myocardium fails to empty the cardiac chambers sufficiently is still unsolved.

Recent experiments pointing toward receptors located in the left atrium, which initiate neurogenic impulses set off by changes in intracardiac blood volume and transmitted to the posterior pituitary, explain only how changes in intrathoracic blood volume can initiate compensatory alterations in blood volume. They furnish no information about the underlying disorder of the myocardium. Several approaches to the role of the heart muscle in congestive failure have been made, all based on the assumption that possible disturbances in the metabolism of the heart in myocardial failure can be detected by a study of the heart's use of substrates; it has been thought possible to find changes in cardiac contractility by observing the contractility or structure of actomyosin.

The problem is particularly difficult, since experimental heart failure, as produced in the animal and the heart-lung preparation, may differ from the failure observed in patients with congestive failure. Spontaneous failure of the isolated heart in the heart-lung preparation occurs within hours after separation of the heart from the rest of the organism. In this type of failure, the contractility of actomyosin remains unimpaired, there is no change in myocardial utilization of substrates, the myocardial oxygen consumption diminishes, and the inclusion of liver and spleen in the perfusion circuit increases cardiac efficiency.[1] In congestive heart failure in man, the myocardial oxygen consumption per unit of weight as well as the use of substrates by the heart does not change, but the contractility of actomyosin bands prepared from failing human hearts obtained at autopsy is diminished [2]; changes in molecular size of the contractile proteins have also been described.[16] This furnishes some clues to the basic mechanism of myocardial failure. A lack of catecholamines in the perfusion fluid may be the cause of spontaneous failure of the isolated heart, while alterations in the molecular structure of contractile proteins, induced by chronic stretch of these fibers, may lead to deficient contraction of the heart in congestive failure.[1] There is as yet a long way to go before the alterations in heart muscle occurring in heart failure are understood. It is likely that heart failure is a protean condition, in which the biochemical changes in the myocardium vary with the underlying cause.

Myocardial Infarction.—In myocardial infarction and hemorrhagic shock, the metabolic changes occurring in heart muscle are much more readily defined. During hemorrhagic shock in dogs the coronary flow diminishes during both oligemic and normovolemic phases.[17] As the oxygen extraction does not increase, the myocardial oxygen usage declines. In the hypovolemic phase of shock, blood levels of glucose rise to high peaks, but this increase in glucose extraction is not statistically significant.[17] Pyruvate extraction falls and negative arteriovenous differences occur frequently. The blood lactate content rises to high levels, presumably as a result of anaerobic glycolysis elsewhere in the body. After retransfusion to a normal blood volume, the myocardial extraction of lactate and pyruvate is depressed similar to that during the hypovolemic state.[17] Blood glucose levels fall to normal with increases in the blood volume. Myocardial glucose extraction is statistically not different from that during the control period; however, in several instances concentrations of coronary vein glucose exceed those in arterial blood. Thus, the essential changes in coronary blood flow and myocardial metabolism in hemorrhagic shock persisted during the normovolemic phase. In both stages myocardial oxygen usage is low and the extraction of glucose, pyruvate, and lactate is impaired. These findings are compatible with those in myocardial ischemia and anoxia.

The metabolic and pathological changes in myocardial infarction have also been clearly defined. Immediately after artificial embolization of the coronary arteries in the dog, the concentration of lactate and pyruvate in coronary vein blood frequently exceeds that in arterial blood. As necrosis progresses, the plasma activity of malic acid dehydrogenase, fructose aldolase, phosphohexoisomerase, and transaminase increases.

The present review has illustrated that study of the physiology and biochemistry of heart muscle on a molecular level can yield valuable information. Much of the work cited above has stemmed from the realization that a purely clinical approach to heart disease is only one aspect of a large field, which needs every means of investigation to advance in the future.

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SPORTS INJURIES OF THE SHOULDER GIRDLE

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Inability to use the shoulder normally can follow a variety of athletic injuries, especially those involving the spinal cord, the brachial plexus, the acromioclavicular joint, the shoulder joint, the clavicle, and the sternoclavicular joint. Exact diagnosis is therefore essential for rational treatment. Understanding of the mechanics of injuries is also essential in designing protective equipment and planning operations to prevent recurrent dislocations. An unusual cause of pain is the displacement of the tendon of the long head of the biceps brachii from its normal location in the intertubercular groove of the humerus. Injuries to the shoulder are not limited to participants in contact sports. Valuable protection is afforded by special training and the use of protective equipment.

Sports injuries of the shoulder girdle are, in general, the common injuries seen in accidents occurring in the routine course of life. However, certain of these injuries occur more frequently in various forms of sport. With use of protective equipment, such as the hat protector in baseball, hockey, and hunting, protection against skull injury is possible to some extent. There is a certain disdain on the part of the athlete toward the wearing of a protective device, but, with time and education, the successful device is willingly accepted. The value of protective devices depends not only on their sound construction but also on the willingness of players to use them.

The incidence of shoulder girdle injuries has been greatly diminished by the development of protective shoulder pads, which have been helpful in the prevention of fracture of the clavicle and dislocation of the acromioclavicular joint. However, sometimes a new protective device may prove satisfactory for its purpose but productive of a new type of injury. The quarterback of our 1947 Rose Bowl team was protected by shoulder pads from an acromioclavicular dislocation, but the pull of the trapezius was transmitted to its insertion on the spine of the scapula, producing a rare fracture detachment of a portion of the spine of the scapula with the trapezius muscle.

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The shoulder girdle has been defined as the arch formed by the clavicle and the scapula. Clinically, however, the soft tissue structures about the base of the neck and the shoulder, and the shoulder joint itself, are included. There are injuries to the neck which are productive of shoulder-girdle symptoms, through neurogenic lesions, and to the muscles which may seriously interfere with function.

Neurogenic Lesions from the Cervical Area

Fractures or fracture dislocations of the cervical spine occur occasionally. The relative infrequency of this type of lesion is a great tribute to the training of athletes, particularly football players and tumblers. Training, to the point of the conditioned-reflex action of Pavlov, in positioning of the head and rolling with the injury plays an important part in the prevention of such injuries. The protective headgear plays a less important part. In my 46 years of experience only one fracture dislocation of the cervical spine has occurred in a varsity football player at the University of Michigan, and this proved not to be serious.

Rupture of the cervical disk is a seemingly unusual but possible injury in athletes. This injury may occur in such an unexpected sport as skeet shooting. The rebound of the gun against the face and shoulder has been known to produce the signs and symptoms of a ruptured cervical disk. I have dislocated my own sternoclavicular joint by shooting at a high duck on the right, so I know that the recoil of the gun can produce a dislocation. The symptoms of rupture of the disk are manifested in the shoulder-arm syndrome and in shoulder-girdle pain. After displacement the disk may protrude laterally, as Semmes and Murphey[1] reported, or posteriorly, into the cord, as reported by Stookey.[2] The neurogenic picture would be one of nerve root damage in the first and of evidence of cord damage in the second type.

Injury to the cervical plexus is possible and not infrequent, particularly in football players. It is rare to have a serious brachial plexus injury occur in a player in a contact sport, but in sports-car or automobile racing it is always a possibility. Damage to the nerve roots by traction produces severe paralysis and sympathetic nerve damage. If this is low in the plexus (at the level of the eighth thoracic segment) there may well be an associated Horner's syndrome, through sympathetic nerve tear. Geographically, just outside of the foramen, injury may occur to the median, lateral, or posterior cord of the plexus.

I have seen one case of brachial plexus posterior cord syndrome develop in a duck hunter, who fell when crossing a small tree bridge and sustained a dislocation of his shoulder. The usual signs of radial palsy and axillary and subscapular nerve involvement substantiated this diagnosis. In this particular instance neuropraxia or physiological injury to the nerve occurred, since complete recovery of muscle function was obtained ultimately.

Peripheral nerve lesions can occur, particularly in body contact games such as football and hockey. More frequently, however, a mild traction occurs, producing so-called neuropraxia, with sudden loss of muscle function in the arm followed by rapid motor recovery. This may develop recurrently in some athletes who charge and block with the shoulder, so that they become temporarily disabled. It becomes a serious matter for coach and football player because of the fear of permanent damage. Usually there is an anatomic reason for such an occurrence, such as a long neck and a narrowed costoclavicular space. More commonly, however, there is evidence of a cervical rib or other bony prominence which can aid in producing pressure on the plexus. I believe that such patients should not continue to participate in a sport which produces recurrent symptoms of this type.

Particular peripheral nerve injuries have been associated with various sports. The long thoracic nerve has reputedly been injured in wrestling, swimming, and tennis, or by endurance hanging tests, with resultant palsy of the serratus anterior. Injury to the suprascapular nerve has been reported in persons participating in acrobatics and bowling. These lesions refer their symptoms to the shoulder girdle and must be differentiated. Usually the lesions are not serious and produce only a brief paralysis. Prevention of these injuries by proper training of players is essential, but, for the patient with a cervical rib, removal from play is advisable if such symptoms develop.

Vascular disorders rarely occur in young players, but it is important to recognize that such lesions may occur in older persons. Congenital aneurysm of the circle of Willis or subdural hemorrhage must be considered, however.

Acromioclavicular Lesions

The acromioclavicular joint is frequently and relatively easily displaced. The separation may be complete or incomplete, depending on the tear of the conoid and trapezoid ligaments. The acromioclavicular ligaments are thin and are easily disrupted in incomplete displacement or subluxation. To produce a complete displacement the strong conoid and trapezoid ligaments must be torn. These ligaments hold the clavicle to the coracoid process, and the acromium is attached to the coracoid by the strong acromiocoracoid ligament. With severe trauma these ligaments may be torn, allowing downward displacement of the acromium with upward displacement of the clavicle. The reverse deformity, with upward displacement of the acromium on the clavicle, is rarely seen.

The prominent location of the acromioclavicular joint facilitates diagnosis through inspection, palpation, and roentgenography. The complete dislocation can readily be observed by the prominence of the distal end of the clavicle, its mobility, and the ease of partial replacement, with immediate recurrence of deformity. Partial or incomplete subluxation produces minimal deformity, readily corrected by light pressure. Roentgenologic diagnosis is more accurate if the patient is sitting when the roentgenogram is taken and carrying weight in the hand on the side of the involved shoulder. Reduction of the deformity must be maintained. Recurrence of the dislocation results if the force of approximation is not continued. In incomplete displacements various types of support, such as Jones[3] or Stimson[4] positioning of the flexed forearm to the clavicle, or the abduction plaster cast method of holding the acromium up to the displaced clavicle, may be used.

The complete dislocation, however, is best treated, in my experience, by open operation. I favor exposing the joint proper, where the acromioclavicular ligaments are often disrupted by the dislocation, with the torn ligaments falling back into the joint and interfering with reduction. The ligaments are freed on reduction of the clavicle into its acromial location. When the reduction has been accomplished, one or two small Kirschner wires are drilled through the acromium into the clavicle under open inspection. This gives excellent fixation. It is reinforced by sewing the torn ligaments together over the acromioclavicular joint. Restoration of the coracoid and trapezoid ligaments is not necessary with this procedure in patients with acute dislocation.

For the treatment of patients with chronic dislocation I developed an operation described independently later by Vargas[5] for reconstruction of these ligaments with the use of the coracobrachialis aponeurosis, cutting a strong fascial segment distally from the coracoid and then turning it back to the posterior superior margin of the clavicle. The acromioclavicular joint previously had been exposed and cleared of scarred, interfering soft tissue and the clavicle securely fixed in place by Kirschner wires through the acromium and the clavicle. This operative technique satisfactorily fulfilled the requirements for restoration of the coracoid clavicular ligaments.

If the joint has become osteoarthritic from long-delayed dislocation, the best method of treatment, in my experience, is Mumford's[6] now classic excision of the clavicle lateral to the conoid ligament. This has proved to be a satisfactory method. The work of Inman and co-workers[7] has substantiated the great value of freedom of motion at this joint rather than arthrodesis.

Prevention of Acromioclavicular Dislocation.—The acromioclavicular joint is so well protected now by shoulder pads that dislocation rarely occurs in members of well-equipped football teams. Instead, I have seen an unusual fracture of the spine of the scapula at the site of insertion of the trapezius. This fracture displaces a small fragment of the spine of the scapula, with the muscle attached. Nonunion is certain, so it is best that the fragment be removed.

In my experience fractures of the scapular body, acromium, and glenoid are rarely the result of sports injuries, unless they are incurred in sports-car accidents or similar severe trauma. Fractures of the coracoid occur so infrequently that they are mentioned as a possibility only.

Dislocation of the Shoulder Joint

Dislocation of the shoulder is a frequent injury in many sports. Often there is a definite history of previous trouble or evidence of a fibroelastic diathesis, which is commonly present in persons with a tendency to dislocation of major joints. The dislocation is usually anterior and frequently subglenoid. It is important to have roentgenograms of the dislocation before reduction so that it can be determined whether it is of the subglenoid or subcoracoid type. This is of diagnostic as well as prognostic value. The capsule is usually torn from the humerus in the subglenoid type, with the head of the humerus penetrating through the torn capsule. In the subcoracoid type the capsule is not torn, but the head of the humerus rides directly over the anterior glenoid margin, establishing a "pocket" into which the head can readily displace under the coracoid process. If roentgenographically the head can be seen directly under the coracoid and anteriorly displaced, it is strong evidence that this is the type prone to recurrent dislocation. The dislocation may be readily reduced, preferably by the Kocher maneuver, with or without intravenous administration of morphine, by careful relaxation of the subscapular muscle. Recurrence of dislocation is not due to failure of the capsule to heal, but rather it points to the two residual, persistent faults occurring after this type of dislocation: (1) a pocket anterior to the glenoid into which the head can go and (2) the compression fracture commonly seen in the posterior surface of the head.

Recurrent dislocation of the shoulder is not infrequently seen bilaterally in athletes. These persons are good athletes because they are unusually limber, with a freedom of joint motion which allows for a greater snap of the wrist and shoulder. The golfer, baseball pitcher, football passer, backstroke swimmer, and wrestler all profit by this increased mobility, but the tendency to dislocation is greater in persons with this fibroelastic diathesis.

Many operations have been designed for the prevention of recurrent dislocation of the shoulder. Since 1947 I have used a combination repair for dislocation of the shoulder, making use of the four essential features stressed in other types of repair. There have been no recurrences in 70 cases. I combine the Nicola[8] with the Putti-Platt[9] and Magnuson-Stack[10] procedures, and, in part, the Hybbinette[11] procedure, to increase the anterior height of the glenoid by an osteotomy of the upper one-fourth of the glenoid rim. This allows the "Putti-Platt half" of the subscapularis and capsule to be sutured to the raw bone under the osteotomy site on fresh bleeding bone and facilitates the passing of sutures through holes made in the hinged flap of bone by a strong tenaculum.

It is rare to see a tear of the musculotendinous cuff in an athlete. A fracture of the greater tuberosity associated with a dislocation is probably a more common injury. Usually the fragments go back into place well after reduction of the dislocation when function returns. If the fragment is displaced medially and not properly in relation to the greater tuberosity, open reduction is advisable.

A common disability of some athletes who use their shoulders excessively, such as baseball pitchers or football passers, is the development of a scapular syndrome, characterized by pain and discomfort on strenuous use of the arm. This syndrome, sometimes called snapping scapula, is one commonly seen in older persons, but it rarely produces more than an annoying pain and discomfort. In these athletes, however, it is greatly aggravated by their powerful efforts, and their efficiency and success are frequently impaired. Anxiety plays a definite part in the disability of both groups, athlete and nonathlete, of those with this syndrome.

The pain is localized primarily in the fifth dermatome, with the vertebral border and superior angle of the scapula being the chief site. Radiation of pain into the neck and the shoulder is frequent. There is a trigger zone at the vertebral border of the scapula just above the spine of the scapula. Usually there is distinct crepitation at the trigger zone site. The rhomboid minor is thick, cord-like, and tender.

Usually, explanation of this lesion and complete understanding of its nature suffices. Local injection of procaine at the trigger zone usually relieves those patients who have persistent difficulty. In the athletes, however, who continually use the arm, I have, on several occasions, found that they were not relieved and their jobs were in jeopardy. I have, therefore, operated on these patients with the concept that local irritation is the result of soft tissue irritation akin to that in the snapping hip. At the junction of the attachment of the aponeurosis of the trapezius to the spine of the scapula and its continuation downward over the edge of the scapula, I have found a thickening of the fascia and a structure consisting of fat and bursa-like tissue on the bony space above the spine of the scapula. The rhomboid minor is thickened and hard near its attachment. I have excised the adipose remnant and freed the rhomboid minor from the scapular edge, suturing it to the fascia over the scapula. It seems most plausible that the soft tissue displacing over the angle of the scapula is the causative factor. I cannot speak authoritatively about the success of this procedure, since I have used it in operations on only a few patients.

Other Injuries

Fractures of the Clavicle.—Fractures of the clavicle are less frequent in football players today, because of the excellent shoulder pads, than formerly, but they are still quite frequent in players of hockey and other body contact games. Because of the severity of the blow the fracture of the clavicle, under such circumstances, is frequently comminuted and extensively displaced. The great desire for activity and early return to function, as well as the displacement and comminution, indicate open reduction and intramedullary fixation in most of these patients who are athletes. I do not usually advocate operative treatment for fracture of the clavicle, however, since healing and good function are the rule with conservative treatment.

Injuries to the brachial plexus are sometimes accompanied or produced by fracture of the clavicle. The clavicular cross is a comfortable and, to my mind, a much more satisfactory type of conservative splinting for clavicular fractures than the figure-eight dressing or the plaster cast. Treatment while the patient is lying down, with the arm in abduction at right angles, is probably the most accurate, conservative method to obtain satisfactory position and minimal callus.

Injury to the Sternoclavicular Joint.—The sternoclavicular joint may be dislocated by minimal trauma. Occasionally the pain and discomfort of the recurrent dislocation of the sternoclavicular joint are so great that it is advisable to correct it by fascial transplants, reconstructing the sternoclavicular ligaments after the abnormal meniscus of the joint has been removed to allow satisfactory reduction.

Bicipital Tenosynovitis.—Slipping of the bicipital tendon in its groove occurs more frequently than most of us have recognized. In older persons tendinitis of the biceps tendon is a frequent cause of shoulder pain and periarthritis. Often rupture of the tendon occurs spontaneously in these patients, seeming to be nature's cure. Hitchcock and Bechtol[12] advocated removal of the long head of the biceps from its groove and cutting of the proximal end of the tendon as near the glenoid labrum as possible. The tendon should then be transplanted into the humerus itself, with a prepared bed from the greater tuberosity fixing it securely in place.

The diagnostic signs of bicipital tenosynovitis are pain, aggravated on abduction and external rotation, and tenderness in the bicipital groove and on rolling the biceps under the examining finger. Resistance against fixed supination and abduction produces soreness. There is evidence that the bicipital groove may be malformed and may often be the seat of the shoulder disabilities. The Sachs-Hill roentgen technique[13] for demonstrating the groove in the humerus is an excellent means of establishing this evidence.

Summary

The shoulder girdle may be injured through nerve damage, joint involvement, fracture, and soft tissue lesion. The therapeutic potential for patients whose lesions are readily recognized is excellent. Proper training of athletes is essential for prevention of these lesions. Persons with malformations of the neck, such as cervical ribs, should be studied; and, if symptoms occur, the person should either have the ribs removed or discontinue participation in sport. Shoulder girdle injuries should be a minimal factor in a well-organized, well-trained, and well-equipped athletic group, with the facilities available today. Dislocation of the shoulder is bound to occur occasionally; it is most difficult to prevent. There may be recurrence if the dislocation is subcoracoid in type. Many of the possible shoulder-girdle injuries have already been prevented by training and support protection.

1313 E. Ann St.

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CLINICAL NOTES

DRIBBLING FROM AN UMBILICAL FISTULA

Samuel R. Newman, M.D., Ralph R. Landes, M.D.
and
Robert B. Eggleston, B.A., Danville, Va.

The continuous dribble of clear acid fluid from an umbilical fistula is not necessarily pathognomonic of a patent urachus. An 8½-month-old child was referred because of an intensely inflamed umbilicus from which clear fluid had dribbled constantly since birth. The history was otherwise noncontributory. Physical examination revealed that the child was normal except for the region of the umbilicus. This was intensely inflamed with a surrounding area of cellulitis. It was covered with a purulent exudate and from the center one observed the slow, constant flow of clear fluid which gave a strongly acid reaction with sodium dinitrophenylazo-napthol disulfonate (Nitrazine) paper. The flow of fluid was carefully observed and aspirated with a pipet as it appeared. The volume measured about 0.5 cc. every 10 minutes.

The tentative diagnosis of a patent urachal duct was made. The patient was placed on penicillin therapy and local hot-wet dressings were applied locally for three days because of the acute inflammatory process. The inflammation subsided in a few days. A cystogram was then performed but failed to delineate any sign of communication with the draining fistula. Water, strongly colored with indigo carmine, was instilled into the bladder, but, to our surprise, the fluid appearing at the umbilicus continued colorless.

The above findings notwithstanding, operation on the patient was performed with the preoperative diagnosis of a patent urachus.

At operation, a 3½-by-1-cm. finger-like tubular structure was found extending directly dorsal from the umbilicus, projecting into the peritoneal cavity. It was unattached to any other intraperitoneal structure. No Meckel's diverticulum was observed.

From Memorial Hospital. Mr. Eggleston is a junior medical student at Harvard Medical School, Boston.

The structure was excised, together with its opening at the umbilicus, and the wound was closed. Convalescence was uneventful.

Microscopic examination of the excised tubular structure revealed it to be lined by stomach and intestinal mucosa. The stomach mucosa showed parietal (acid-secreting) cells. Sections through the wall of the specimen showed typical intestinal musculature. The pathological diagnosis, therefore, was omphalomesenteric duct remnant containing acid-secreting gastric mucosa.

Comment

When the omphalomesenteric duct fails to become obliterated, several conditions may result: 1. The most common condition, failure in obliteration of its proximal portion, results in Meckel's diverticulum. 2. Closure at both its proximal and its distal portion, with failure to close at its midpoint, results in a vitelline duct cyst. 3. Complete failure of closure results in an umbilicointestinal fistula. 4. Closure proximally but failure to close distally results in an omphalomesenteric fistula such as in the present case.

Each of these variations contains differing amounts of intestinal and/or gastric mucosa. Meckel's diverticulum is variously reported as containing gastric mucosa in 12 to 52% of the cases,[1] either alone or with intestinal mucosa. It was thought by Nicholson that this tissue originated in situ by an abnormal differentiation of the cells of the entoderm rather than as a displacement of the epithelium of the stomach.[2]

An omphalomesenteric fistula secreting acid is rare. In Cullen's classic treatise[3] only seven cases are reported. Cases have also been mentioned by Aitken[4] and Gross.[5] More recent reviews do not report any cases of this type.[6]

Summary

An omphalomesenteric duct continuously secreting a clear acid fluid was mistakenly considered to be a patent urachus draining urine. It was only at operation that the structure was recognized and that the fluid was identified as gastric juice.

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CLINICAL SCIENCE

RESEARCH AND COMMON SENSE IN A CLINICAL SPECIALTY—ANESTHESIA

Henry K. Beecher, M.D., Boston

In an exact sense there is no such thing as clinical science, and there is no science of anesthesia. Anesthesia is an aggregation of clinical techniques built on several sciences, among others pharmacology, physiology, biochemistry, physical chemistry, and physics. Anesthesia is not a science, which is one of several reasons why I object to the term anesthesiology, meaning science of anesthesia. There is, however, a better reason than the semantic one for laboring this point, for herein lies the clue as to where research fundamental to the growth of the field is bound to occur; that is, in the basic sciences. Anesthesia greatly needs investigators capable of working in the basic sciences. As long as anesthesia (or any other specialty) leads a parasitic existence, scientifically speaking, depending as it does almost wholly on scientists in other fields for fundamental developments, it can hardly have much stature among other and stronger medical disciplines.

The Greatest Threat

Let it be granted that the greatest single threat to the specialty of anesthesia is the possibility—the actuality in too many places—that the anesthetist will fail to participate in medicine as a whole, forgetting that he is first physician and second anesthetist. The individual doctor may indeed carry out research in anesthesia, but if his work has significant value it is likely to be better characterized as research by an anesthetist, a nice distinction made about surgery by Edward D. Churchill in

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From the Anesthesia Laboratory of the Harvard Medical School, Massachusetts General Hospital.

his recent Lowell lecture. The breadth implied not only enriches the field but serves to attract able young men to it, a critical need in the field of anesthesia. Just as the internist is the physiologist in the clinic, so also the anesthetist can be the pharmacologist. It is essential that there be continuous communication between the specialties and the parent disciplines. Anesthetists need to participate in the medical life of their community. They can do this especially through research, if it is fresh and original. The anesthetist will never be a significant part of the medical scene unless he promotes its growth. To live at all is to grow. The alternative is at least a moribund state and rejection by the body of medicine.

Mechanical Development Versus Fundamental Growth

I have no objection to a preoccupation on the part of some with machines; this may best suit their talents and it has surely led to useful developments in the past and doubtless will in the future. One can object, however, to a confusion of such activity, however needful, with fundamental research. New concepts are the basic stuff from which significant research comes. There is in anesthesia, on the part of those who should know better, a curious hostility to what might be called interest in concepts. I can illustrate this by a wry experience I had while carrying out an examination. As long as questions were limited to "factual" matters (e. g., how many gallons of nitrous oxide are contained in a G-sized cylinder under specified conditions) all was well, but if I shifted to a question dealing with concept, trouble was at hand. I unfortunately once asked a potential specialist to discuss the physical and biological characteristics of the ideal inhalation agent, a "concept" which can be expressed in the most explicit terms. (It is of interest to learn that, since that time, this question is now one commonly asked of candidates.) The evident alarm on the face of the one examined was supported by a well-known fellow examiner, who abruptly left the room. One can be sure of this: There will be no enduring growth unless basic concepts are recognized and understood and new ones developed. It would be interesting to make a list of the principal ones in anesthesia.

Courses for "Training in Research."—It is curious that courses are offered in techniques of research for anesthetists with no special problem in mind. In a reasonably long association with scientists, I have never known, or even heard of, a single scientist of consequence who started out by taking a general training course in research methods, except when such training was directed by a respected scientist (the master-disciple relationship) to a specific end. Sometimes self-starters in research have independently taken courses directed toward helping solve a given problem, but these were not unmotivated courses in "training in research methods." If courses in training in research were really useful, surely this fact would have been discovered long ago in other disciplines, and yet no known scientist has developed in this way. It seems most improbable that anesthetists, generally inexperienced in research, will find such courses useful.

The Promotion of Fundamental Growth.—I have expressed disbelief in the usefulness of so-called training courses in research, unless they are motivated by a specific need. If such courses are disallowed, how then is research to be promoted? Perhaps the matter can first be usefully approached through indirection.

Some time ago I received a letter from an anesthetist, which read, "I have bought an oximeter; will you suggest a research problem to use it on?" This seemed funny at the time. The humor has long since given way to startled recognition that this was no isolated attitude but, incredible as it may seem, a not uncommon approach to research in anesthesia. Nowadays the oximeter has been supplanted by exceedingly complex—and expensive—electronic equipment. All too often the attitude, although unexpressed, seems to be: first, the machine (the more it glitters, the better) and, second, the idea. Emphasis is on the material, on machines (one hesitates to say on gadgets, but that is what they often are) and technique rather than on a search to discover the elemental problems and needs for anesthesia's growth.

Visits to many anesthesia laboratories show that these often contain elaborate and costly electronic devices which, on inquiry, one learns are "being calibrated"; rarely are they in use in a well-designed study. Further inquiry as to "then what?" leads all too often to a vague reply which clearly reveals that the costly machine was in reality the end in itself and that no bold new concepts were on hand for testing. The preoccupation is once again with the machine, not with an idea.

My former teacher, August Krogh, carried out his celebrated work with only a microscope and a few homemade pieces of apparatus. He was nevertheless honored by a Nobel prize. He once expressed the view that obstacles should be placed in the way of those who showed an interest in doing research, and then, if they persisted and finally overcame a series of formidable difficulties placed in their path, they might perhaps be given a trial at investigation, but certainly no expenditures for elaborate equipment would be made then or for years to come. This might be called the aristocratic view of the investigator. There is, indeed, room for another approach. It has been expressed by Ramon y Cajal, also a Nobel laureate, whose view was surely colored by sad thoughts of the low state of Spanish science. Cajal believed that many should be encouraged to go into scientific research. He recognized that there would be few men with the intuitive power and originality which characterize the true scientist, but he likened science to an army, in which there are places for foot soldiers, corporals, and colonels, but only a few generals. This proletarian *attitude as opposed to Krogh's aristocratic* one is closer to that now prevalent among anesthetists, who seem almost universally to hold the view that everybody should do research. The consequences of this are evident in much worthless stuff which finds its way into print, and the clutter grows mightily.

It is my conviction that no physician should be allowed to tie up large sums in complex equipment until he has demonstrated that he can first make a significant contribution to knowledge, with no more equipment than a notebook and pencil—and an idea—and such simple apparatus as he can build himself.

Funds are sought in anesthesia and, remarkably enough, granted "for training others in research" by men who have themselves done no significant research. Unfortunately, persistent attention to a given problem is uncommon among young clinical investigators. One can only deplore the frequent mad scramble from band wagon to band wagon in the name of research. While this compulsion is not limited to it seems to be especially prominent in the field of anesthesia.

What is the road to progress? While the young investigator must discover in himself his talents and interests and must determine the facilities and opportunities his environment contains, and all this may lead early in his career to brief appearances in several fields, the dedicated investigator will pursue one chief problem for years.

The anesthetist, like all other investigators, must seek useful new concepts, if his research is to be fruitful. His primary concern will be the discovery and establishment of such concepts. It seems most unlikely that current preoccupation with machinery or even unmotivated general "courses for training in research" will promote this end. It is scarcely possible to think of any path "out of the wood lot" other than by the apprenticeship of a relatively few young men to scientists and support of them by means of research grants. Such men must participate in, but have freedom from, the crushing clinical load common to workers in the field of anesthesia.

PRELIMINARY COMMUNICATIONS

EFFECTS OF LARGE INFREQUENT DOSES OF A-METHOPTERIN ON ACUTE LEUKEMIA IN CHILDREN

Paul T. Condit, M.D., Ph.D.
and
Leonard P. Eliel, M.D., Oklahoma City

The importance of dosage in the treatment of mouse leukemia with a-methopterin (Methotrexate) has been demonstrated by Goldin and associates.[1] They found in the treatment of leukemia L 1210 that a schedule of large, infrequent doses of a-methopterin was, with regard to survival time, therapeutically superior to single maximum doses or to small, consecutive daily doses, if treatment was begun soon after tumor implantation. The optimum interval of four days between consecutive doses was subsequently shown to be closely related to the time required for recovery of the mouse from the effects of the drug.[2] The enhanced therapeutic effectiveness of this intermittent regimen suggested that the host recovered faster than the tumor, so that the tumor was damaged selectively by subsequent doses of the drug.

The therapeutic advantage of this dosage regimen was so obvious that its clinical application was undertaken. Studies in man led to the selection of a dosage schedule of a-methopterin of about 5 mg. per kilogram of body weight, repeated at intervals of about two weeks.[3] This dosage regimen of a-methopterin did have some antitumor action in adult patients with solid tumors.[4]

To compare the effectiveness of different dosage schedules of antitumor drugs, a tumor should be selected which responds with some regularity to the drug under study. The diseases of human beings which respond to a-methopterin are choriocarcinoma found in women and acute lymphoblastic leukemia of childhood. Hertz and associates[5] have demonstrated the effectiveness of an intensive dosage regimen of a-methopterin in the treatment of choriocarcinoma. The treatment of acute leukemia also has been attempted with an intermittent dosage regimen, but the doses used in that study were too small and the interval between consecutive doses was too short for optimum therapeutic results.[6]

This report deals with the results of a-methopterin treatment in three child patients with acute lymphoblastic leukemia, who had been placed on a

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From the Oklahoma Medical Research Institute.

his recent Lowell lecture. The breadth implied not only enriches the field but serves to attract able young men to it, a critical need in the field of anesthesia. Just as the internist is the physiologist in the clinic, so also the anesthetist can be the pharmacologist. It is essential that there be continuous communication between the specialties and the parent disciplines. Anesthetists need to participate in the medical life of their community. They can do this especially through research, if it is fresh and original. The anesthetist will never be a significant part of the medical scene unless he promotes its growth. To live at all is to grow. The alternative is at least a moribund state and rejection by the body of medicine.

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and
Leonard P. Eliel, M.D., Oklahoma City

The importance of dosage in the treatment of mouse leukemia with a-methopterin (Methotrexate) has been demonstrated by Goldin and associates.[1] They found in the treatment of leukemia L 1210 that a schedule of large, infrequent doses of a-methopterin was, with regard to survival time, therapeutically superior to single maximum doses or to small, consecutive daily doses, if treatment was begun soon after tumor implantation. The optimum interval of four days between consecutive doses was subsequently shown to be closely related to the time required for recovery of the mouse from the effects of the drug.[2] The enhanced therapeutic effectiveness of this intermittent regimen suggested that the host recovered faster than the tumor, so that the tumor was damaged selectively by subsequent doses of the drug.

The therapeutic advantage of this dosage regimen was so obvious that its clinical application was undertaken. Studies in man led to the selection of a dosage schedule of a-methopterin of about 5 mg. per kilogram of body weight, repeated at intervals of about two weeks.[3] This dosage regimen of a-methopterin did have some antitumor action in adult patients with solid tumors.[4]

To compare the effectiveness of different dosage schedules of antitumor drugs, a tumor should be selected which responds with some regularity to the drug under study. The diseases of human beings which respond to a-methopterin are choriocarcinoma found in women and acute lymphoblastic leukemia of childhood. Hertz and associates[5] have demonstrated the effectiveness of an intensive dosage regimen of a-methopterin in the treatment of choriocarcinoma. The treatment of acute leukemia also has been attempted with an intermittent dosage regimen, but the doses used in that study were too small and the interval between consecutive doses was too short for optimum therapeutic results.[6]

This report deals with the results of a-methopterin treatment in three child patients with acute lymphoblastic leukemia, who had been placed on a

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From the Oklahoma Medical Research Institute.

regimen of parenterally administered doses of from 1 to 5 mg. per kilogram of body weight (20 to 105 mg.), repeated at intervals of from two to four weeks.

Report of Cases

CASE 1.—The first patient was a 6-year-old girl who had been treated with adrenocortical steroids and 6-mercaptopurine. She had experienced a prolonged remission but had relapsed 14 months after diagnosis. Even though an immediate hematological response was apparent after 1 dose of a-methopterin had been given, complete remission[7] was not achieved until 8 doses of the drug had been given over a period of almost six months. During this time, while clinically free from leukemia, she had a prolonged period of anorexia, emesis, and emaciation, apparently due to treatment with a-methopterin. The patient's course was complicated by infiltration of the central nervous system with leukemia, which responded, however, to intrathecal administration of a-methopterin and x-ray therapy. When, after six months, a-methopterin therapy was discontinued, the remission continued for only two months before hematological relapse occurred. Re-treatment with a-methopterin induced a second transient, partial remission but failed to prevent her death from leukemia two months later (24 months after diagnosis). This patient's entire course of treatment with large, intermittent doses of a-methopterin lasted more than 10 months, and she was in complete or partial remission during most of that period.

CASE 2.—The second patient was a two-year-old boy who had been suffering from acute lymphoblastic leukemia for eight months prior to the onset of the therapy under discussion. During this period he had been given hydrocortisone, 6-mercaptopurine, a-methopterin, and combinations of a-methopterin and 6-mercaptopurine. While good clinical remissions had been obtained, the hematological remissions had been partial and transient. At a time when the patient was in partial clinical (but not hematological) remission, a-methopterin was administered in doses of from 2.5 to 5.0 mg. per kilogram of body weight (35 to 75 mg.), at intervals of from two to four weeks. Clinical remission became apparent after 6 such doses; complete remission appeared after the 8th dose and was maintained for about one month. Continued treatment with a-methopterin maintained a partial hematological although complete clinical remission for an additional month before relapse, leading to his death one month later (15 months after diagnosis), occurred. This patient's entire course of treatment with large, intermittent doses of a-methopterin lasted seven months, and he was in complete or partial remission during most of that period, despite the fact that he was refractory to conventional a-methopterin therapy.

CASE 3.—The third patient was a six-year-old girl who had achieved an initial remission with prednisone (Meticorten) therapy and was then maintained on therapy with 6-mercaptopurine until she relapsed 20 months after the onset of her disease. Since she had failed to respond to administration of 3 doses of a-methopterin of from 1 to 4 mg. per kilogram of body weight (20 to 80 mg.) at intervals of two weeks, she was re-treated with prednisone. A complete remission resulted, which lasted about two months, when she relapsed again and was treated with a-methopterin in doses of from 4 to 5 mg. per kilogram of body weight (75 to 105 mg.). After 3 such doses, a clinical and hematological remission began, but, like the first patient, she also experienced a prolonged period of anorexia, emesis, and emaciation, apparently due to intensive a-methopterin therapy, at a time when there was no evidence of active leukemia. Her course was complicated by staphylococcic septicemia. A subsequent dose of 4 mg. of a-methopterin per kilogram of body weight (75 mg.) produced a normocytic hypoplastic anemia, which led to a fulminating septicemia due to Pseudomonas aeruginosa and to death on the 13th day after administration of the drug (27 months after diagnosis). This patient initially had failed to respond to therapy with a-methopterin but ultimately started into remission after larger doses were used. Her death was due to overwhelming infection at a time when a drug-induced normocytic hypoplastic anemia was present and the leukemia was clinically suppressed, although it was still in evidence at postmortem examination.

Comment

One other child with acute lymphoblastic leukemia is currently under treatment with a-methopterin, but results cannot be evaluated at this time. One child with acute monocytic leukemia failed to respond to this or any other treatment.

The three patients described here had each received prolonged antileukemic therapy of the conventional type, but only one was resistant to folic acid antagonists. The remissions produced by this regimen of large, intermittent doses of a-methopterin have been satisfactory and, in one instance, unexpected. In each case a number of doses was necessary to produce the remission. In the first patient the importance of continuing therapy was demonstrated, because a prompt relapse occurred when a-methopterin therapy was discontinued. To achieve remission, a prolonged period of hospitalization was necessary, during a large part of which all three children were critically ill.

These preliminary studies on the value of a-methopterin therapy in children with acute lymphoblastic anemia have been concerned primarily with determination of the size of individual doses, the interval between doses, and the number of doses required to produce a therapeutic response. With more experience it is probable that remissions can be achieved sooner and with less toxicity than occurred in these patients.

These results indicate that, as in the mouse, this dosage regimen of a-methopterin has an antileukemic action. Additional patients and a longer period of observation will be required to assess the relative effectiveness of this regimen as compared with the more conventional schedule of administration of small, consecutive daily doses of a-methopterin.

Our observations suggest that this treatment may be helpful in the management of children with acute leukemia which is refractory to the usual forms of therapy. Use of a-methopterin in this fashion must be advocated with caution, however, because the present series of patients is too small for accurate prediction of appropriate doses. For example, a dose that was innocuous in some children produced severe toxicity in others. The reasons for these variable responses are not yet clear.

825 N. E. 13th St. (4) (Dr. Eliel).

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SPECIAL CONTRIBUTION

ADVERTISING IN THE A. M. A. SCIENTIFIC PUBLICATIONS

The American Medical Association seeks to promote the science and art of medicine and the betterment of public health. In serving these aims, the A. M. A. communicates regularly with the members of the medical profession, with professional persons in allied fields, and with the public. A substantial part of this communication is carried on through the regular production and distribution of several publications.

In keeping with its avowed purposes, the Association will do all it reasonably can to ensure the accuracy, comprehensiveness, timeliness, and relevancy of the advertising content of these publications. The evaluation of advertising copy will be based on the consideration of available data concerning the product or service. It will not be based on tests conducted by the A. M. A.

The appearance of advertising in A. M. A. publications should not be construed as a guarantee or endorsement of the product by the Association. The fact that an advertisement for a product, service, or company has appeared in an A. M. A. publication shall not be referred to in collateral advertising without specific authorization from the Advertising Committee.

As a matter of policy, the A. M. A. will sell advertising space in its publications when (1) the buyer believes purchase of such space represents a sound expenditure; (2) the inclusion of advertising material does not interfere with or seriously detract from the purpose of the publication; and (3) the advertising copy meets the standards established for such publication.

I. General Principles Governing Advertising in A. M. A. Scientific Publications

The following general principles are criteria which the Advertising Committee will follow in screening advertising to be carried in the A. M. A. scientific publications (The Journal and the 10 Specialty Journals). The Association reserves the right to change these principles in the light of developments in medicine or in industry. The A. M. A. Advertising Committee for scientific publications makes the final decision regarding the eligibility of all products and services to be advertised in the Association's scientific publications.

A. Eligibility for Advertising

1. Products or services eligible for advertising shall be germane to, effective in, and useful in the practice of medicine and shall be commercially available.

2. Pharmaceutical products will not be eligible for advertising until a New Drug Application from the Food and Drug Administration has become effective.

3. "Institutional-type" advertising germane to the practice of medicine and "public service" messages of interest to physicians may be considered eligible for appearance in the scientific publications.

4. Alcoholic beverages and tobacco products are not eligible for advertising.

5. The Association may decide that certain products or services are not eligible for advertising in A. M. A.'s scientific journals if advertisements for these products or services in other mediums consistently, or significantly, depart from the standards set forth in the following section.

B. Suitability of Advertising Copy

After a product or service has been declared eligible to be advertised in the scientific publications of the A. M. A., the Advertising Committee must approve each advertisement. As in the case of eligibility, the Committee makes the final decision regarding the suitability of copy, layout, and art work. The Committee's decisions on these matters will be guided in all cases by the following principles:

1. The advertisement should clearly identify the advertiser and the product or service being offered. In the case of drug advertisements, the full generic name, including salt and ester designation, of each active ingredient must be shown in appropriate type size. If the generic name of a drug appears in close juxtaposition to the trade name, it should not be unduly subordinated and under no circumstances appear in less than 8 point type. If the generic name does not appear in close juxtaposition to the trade name, it should not be unduly subordinated and under no circumstances appear in less than 10 point type.

2. Advertisements should not be deceptive or misleading. Layout, art work, and format should be such as to avoid confusion with the editorial content of the publication.

3. Unfair comparisons or the blatant and unwarranted disparagement of a competitor's products or services will not be allowed.

4. Sweeping superlatives or extravagantly worded copy will not be allowed. Any claims for superiority must be supported by evidence acceptable to the Association.

5. Quotations or excerpts from a published paper are acceptable only if they do not distort the meaning intended by the author. Claims made within quotations must conform to the same standards as unquoted claims.

6. Advertisements will not be accepted if they appear to conflict with the principles of medical ethics.

C. Procedures of the A. M. A. Advertising Committee (*Scientific Journals*)

The A. M. A. Advertising Committee is responsible for applying the foregoing principles and standards to advertising copy submitted for publication in A. M. A. scientific journals. It will do so in accordance with the following procedures:

1. *Submission of Data.*—The Advertising Committee requires that scientific data be submitted to substantiate claims made for new products (such as drugs, devices, or foods) or new claims for products which have previously appeared in A. M. A. scientific journals.

2. *Type of Data Needed.*—Data should include pertinent reports, published and unpublished, favorable and unfavorable, of laboratory and clinical investigations covering the efficacy and relative safety of the product (drug, device, or food) under consideration. These data should be based upon sound studies and should be sufficiently comprehensive to permit a critical evaluation of the subject matter. While the quantity of the scientific data required will depend on the type of product, the nature of the medical problem involved, and the claims made in the advertising copy, the *quality* of the evidence is regarded as highly important; in this respect, the importance of suitable controls is emphasized. Compilations of individual case reports are ordinarily not considered acceptable evidence. The unpublished portion of all submitted data will be regarded by the Advertising Committee as confidential, and consultants will be requested to treat it accordingly.

3. *Consultation.*—The A. M. A. Advertising Committee frequently seeks the opinions of consultants and recognizes the statements formulated by A. M. A. Councils and Committees in determining the eligibility of products and the suitability of claims. The consultants for the Advertising Committee are persons who have been selected for their competence in the field involved. Names and affiliations of the consultants are not made available.

D. Advertisements for Specific Types and Classes of Products and Services

1. *Drugs.*—For convenience, advertisements for drugs (including vaccines and biologicals) may be separated into four categories, as follows.

(*a*) New Drugs or New Claims for Drugs Which Have Not Previously Been Advertised in A. M. A. Publications: A new drug is here defined as a single active ingredient (examples: reserpine, deserpidine) or an extract from a single source (examples: alseroxylon, rauwolfia). Example of a new claim: use of an established antimalarial drug, such as chloroquine phosphate, in rheumatoid arthritis. In all such cases, the Advertising Committee will require six copies of supporting scientific evidence for review. It is suggested that laboratory and clinical data on new drugs be submitted to the American Medical Association at the time a New Drug Application is filed with the Food and Drug Administration. This will make it possible, in many cases, to obtain product and advertising clearance prior to the introduction of the drug. However, the Association will not grant final clearance of advertising until notified that the New Drug Application has been made effective by FDA.

(*b*) Drugs Which Represent a Modification of an Eligible Product: Example: Some modification of a previously eligible drug such as a new salt or ester. Six copies of all pertinent laboratory and clinical data should be forwarded to the Advertising Committee.

(*c*) Mixtures of Drugs Which Are Already Considered Eligible: For example, a mixture of reserpine and amphetamine was regarded as new at one time. Six copies of clinical and pharmacological data should be forwarded for consideration by the Advertising Committee. Clearance depends primarily on showing justification for the rationality of the combination.

(*d*) Drugs Which Represent an Additional Brand of a Product That Is Already Eligible: Nothing further is needed than the proposed advertising copy for consideration by the Advertising Committee.

2. *Apparatus, Instruments, and Devices.*—The Advertising Committee determines the eligibility of products and suitability of claims for medical equipment intended for preventive, diagnostic, or therapeutic purposes. Advertisements for new products and new claims should be accompanied by six copies of information presenting full and adequate scientific and technical data concerning the product's safety, operation, and usefulness, including the results of laboratory and clinical examination. These data may be either published or unpublished. Samples of apparatus, devices, equipment, or instruments should not be submitted unless specifically requested by the Committee.

3. *Food Products and Vitamin Preparations.*—Advertisements for food products and vitamin preparations may be separated into four categories, as follows:

(*a*) General-Purpose Foods: Those foods promoted for use by the population in general. Examples would be fresh oranges, bread, meats, eggs, and processed fruits and vegetables. Advertisers of such products should submit six copies each of descriptive literature, labels, and a statement of composition.

(*b*) Special-Purpose Foods: Those foods manufactured and promoted for use by certain specific segments of the population, such as infants, invalids, and others requiring foods with certain properties. Examples would be strained and chopped foods for infants, foods for carbohydrate-restricted diets, and foods for sodium-restricted, fat-restricted, and other therapeutic diets. Advertisers of such products should submit six copies of labels, statement of composition, analytical data, and clinical data, demonstrating the effectiveness and safety of the product for its intended use. If new claims are made for a previously advertised product, six copies of clinical data substantiating such new claims must be submitted.

(*c*) Supplemental Vitamin Preparations: Rational mixtures of the vitamins recognized to be essential in human nutrition or metabolism in amounts not differing greatly from the recommended dietary allowances of the Food and Nutrition Board of the National Research Council are eligible. However, with the exception of iron-containing and calcium-containing preparations that are intended for use during pregnancy, vitamin mixtures to which minerals are added (as contrasted to trace minerals which are inherent in the manufacturing process) are not eligible for advertising.

(*d*) Therapeutic Vitamin Preparations: Rational mixtures of the vitamins recognized to be essential in amounts not greater than five times the recommended dietary allowances are eligible. However, preparations containing a mixture of all or most of the following antianemic factors — vitamin B_{12}, folic acid, intrinsic factor, iron, ascorbic acid, and copper—are not eligible for advertising. If claims not generally recognized are made for any of the vitamins, or mixtures of vitamins, such claims shall be substantiated with six copies of clinical studies in support of such claims.

4. *Cosmetics.*—For cosmetics with acknowledged sound health claims, only the qualitative formula need be given. In the event that a question of safety arises, quantitative data on the one or more ingredients in question are necessary. In the case of a new cosmetic, or a cosmetic to which new ingredients have been added, six copies of supporting data for the product's safety and ability to perform as claimed should be forwarded to the Advertising Committee for review. Since relevancy to medical practice is one of the prerequisites for eligibility, it should be emphasized in each advertisement.

5. *Books.*—A book may be requested for review so that its eligibility for advertising may be determined.

6. *Miscellaneous Products and Services.*—Products or services not in the above classifications may be eligible for advertising if they satisfy the criteria for eligibility and suitability.

II. Time Requirements for Advertising Committees

Although the Advertising Committees cannot guarantee adherence, in all cases, to a fixed time schedule, every effort will be made to expedite completion of Committee consideration in the following time intervals:

Advertisements for Eligible Products with No New Claims.—From the time copy is received, five working days should be allowed for Committee consideration.

Advertisements Involving New Claims for or Modifications of Currently Eligible Products, or Both.—From the time copy and, if necessary, supporting data are received, 15 working days should be allowed for Committee consideration.

Advertisements for New Products.—From the time copy and supporting data are received, 20 working days should be allowed for Committee consideration. In those cases in which Committee consideration cannot be completed prior to the expiration of the foregoing time intervals, the advertiser or agency will be so informed.

THE JOURNAL
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STANDARDS FOR ACCEPTANCE OF ADVERTISING

"THE TRADE of advertising is now so near perfection, that it is not easy to propose any improvement. But as every art ought to be exercised in due subordination to the public good, I cannot but propose it as a moral question to these masters of the public ear, whether they do not sometime play too wantonly with our passions." Thus wrote Samuel Johnson 250 years ago, according to his biographer, James Boswell.

A documented set of standards for acceptance of advertising in A. M. A. scientific periodicals has been compiled. It appears in this issue. The need for a carefully prepared and succinctly defined code needs little elaboration. Prior to 1955 a stamp of approval was required for each product advertised in A. M. A. scientific publications. The abandonment of the stamp of approval did not mean abandonment of critical review of advertising copy submitted; quite the contrary. Rigid standards for acceptance have been maintained, and editing of even modest claims has been customary. From time to time, the Advertising Committee has called on qualified medical consultants to assist them in evaluating the merits of advertised products and the accuracy of the claims made. This function of the Association is not generally appreciated, especially by many physicians who are as deeply interested in the quality and quantity of advertising as in the scientific contents of the journals.

Advertising in medical periodicals is a matter second in importance only to the scientific contents. A review of suggestions regarding the function and mission of the scientific publications of the A. M. A. that have been received in recent months amply substantiates its importance. This is not surprising when one compares the size of an issue of The Journal in 1960 with that of one from the 1930's or even the 1940's.

The communication in this issue of The Journal is recommended reading. The Board of Trustees approved these principles at the Clinical Session in Dallas.

The Standards for Acceptance apply only to The Journal and to the Specialty Journals published by the A. M. A. They are not concerned with the advertising policy in *Today's Health* or the *A. M. A. News*. A companion statement of procedure is being formulated for these publications. It is anticipated that it will be equally firm.

THE INTERMEDIUM OF INFORMATION

Where should the physician forage for the latest information on what is new in medicine? Frequently the editor of a conservative medical journal is overwhelmed with indecision about accepting a manuscript prematurely, and running the risk of indiscretion, or waiting until all of the evidence is at hand, at which time the reading public, including the physician, is well informed. Somewhere in the land of perplexity there must be a cay of compromise so that the physician will not be forced to rely on the medicine section of *Tempo* or *Wochenblatt* to learn the latest.

Several devices have been suggested to alter the present unsatisfactory situation. Two of these have been discussed at sufficient length to warrant mention. The Journal will be receptive to manuscripts known in laboratory parlance as preliminary communications. These must be short in length and clear in presentation of a single fact or a group of related facts that have been subjected at a late date to critical study and found valid, thus leading to an apparently logical conclusion. A kindly eye will also be cast on manuscripts describing something new in basic science or clinical science. Neither the requirements nor the length will be as rigid. The communications to be included in the section titled Clinical Science should be descriptive, without ponderous scientific terms and without benefit of confusing tables or complicated graphs. In each instance these will be signed communications.

In this issue of The Journal the first manuscript in Clinical Science, prepared by Henry K. Beecher, a member of the Council on Drugs, is published, as well as the first item in the section *Preliminary Communications*, by Condit and Eliel, from the Oklahoma Medical Research Institute. Your evaluation, in a letter to the editor, of this type of contribution will be helpful in adjudicating future policy.

THE NEEDY AND THE NEAR-NEEDY PHYSICIAN

In contemporary times, when much thought has been or should be given by physicians to the proposals advanced in the Forand resolution, let us not overlook the physician who may be in need of financial aid. The application of the federal proposal is confined to citizens over 65 years of age. The title of this editorial implies no temporal restriction. A physician in need of provisional or long-term aid may be a recent graduate of medical school stricken with poliomyelitis or a physician no longer able to practice because of age or chronic illness.

The medical profession in some states has grappled with the problem squarely and has responded with a plan of action. States with the largest physician population have accepted their responsibilities for a long period of time. The California Medical Association underwrites a nonprofit corporation which provides benefits for needy physicians and their families. The fund is supported by a contribution of one dollar a year from the dues of each active member of the association. In the southern part of the state the Los Angeles County Physicians Aid Association was incorporated in 1940. This association provides either direct financial aid or domiciliary care, depending on the circumstances. The state medical society in Illinois established a benevolence fund in the same year. Direct monetary aid is provided. There is no specifically designated physicians home. The Massachusetts Medical Benevolent Society was organized in 1857 with the provision for direct aid to indigent physicians and their widows. In New York state, the Physicians Mutual Aid Association was incorporated in 1868 with a purpose similar to that of the Massachusetts society. A proposal for a physician's home was given a trial in the 1920's but abandoned in favor of direct monetary aid.

This information has been gleaned from a brochure on the subject which was prepared by Beverly C. Smith of New York City. The contents were assembled after an inquiry to the executive secretaries of the constituent medical societies throughout the country. C. Gordon Heyd, past-president of the American Medical Association, is the president of the New York organization. The brochure supplies helpful documentary data for one interested in this matter, a subject reviewed by the House of Delegates at their recent session in Dallas. The resolution submitted by a delegate of the Indiana State Medical Society requests that "The American Medical Association take appropriate steps to investigate the need, the desirability, and the feasibility of establishing a suitable facility in a suitable climate as an abode for aged and aging physicians and for those who have retired from the active practice of medicine." The Reference Committee acted favorably on this resolution, which was supported by the House of Delegates. It is believed that this measure is one approach to a problem that will be applicable to a small percentage of physicians only, but it is pertinent until such time as a voluntary physicians' annuity program is approved. Furthermore, maximum benefits of a group retirement annuity plan for physicians will be possible only if legislation similar to HR-10, 86th Congress, as approved by the House of Representatives in March, 1959, and now pending before the Senate Finance Committee, is passed.

Through one device or a combination the physician in financial need must be reassured just as he has comforted countless patients during his days of professional activity.

FORCED RESEARCH

Since this reward and those linked with research grants (travel, secretarial help, and freedom from teaching) combine lucre with glory, it is not surprising that inside the university and on its industrial and other fringes the practice or pretense of research should have become a compulsion. Thousands of young men are at work on little papers; thousands more are wracking their brains to think of an experiment or study. Most of them worry more about the acceptability of the subject in academic eyes than about their chances of doing and saying something useful, that is, few care about the fitness of the matter and none about the readability of the results. "Communication" occurs by good luck, while everybody groans ritually at the bad writing, excessive length, and prevailing insignificance of what the journals print. In a word, this army of researchers by conviction or impressment are technically pedants.—J. Barzun, The House of Intellect, New York, Harper, 1959.

CHANGE OF ADDRESS

If you change your address please notify THE JOURNAL at least six weeks before the change is made. Include the address label clipped from your latest copy of THE JOURNAL, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

On entering this new decade of the 1960's I foresee a host of significant challenges to the medical profession. For example, because of our rapidly expanding population the need and demand for more physicians must be met. We also know that scientific advances in health maintenance, treatment, and care may push patients' expenditures upward; therefore, we must make a concerted effort to hold medical costs at reasonable levels.

These are just two important challenges. You undoubtedly have several others in mind. By far the most urgent and crucial challenge is the defeat of the proposed federal control of medical care for the aged under the Forand bill. The passage of any such legislation this year, or at any time, would be the beginning of complete political medicine in the United States.

For months now I have talked about this issue throughout the country. Whenever I discuss it, I try to answer some of the basic questions concerning the Forand bill, which proposes to give a limited amount of hospital, surgical, and nursing home treatment to some 16 million people eligible for Social Security retirement and survivorship. Here are some of those questions and answers. I hope they will help you in your discussions of the measure with friends, neighbors, and patients.

Q. What would such a federal program cost?

A. About 2 billion dollars a year—for the first and second years of operation. After that costs probably would skyrocket—as they did in Great Britain.

Q. Who would pay the bill?

A. Everyone who pays Social Security taxes. These taxes already are scheduled to reach 9% of payroll in the years ahead. This means that a tax of $216 on income of $4,800 a year will be paid, with the employer also paying $216. The Forand bill would cut take-home pay even more, by further increasing the rate of Social Security tax.

Q. Is the Forand bill necessary?

A. No. Health insurance has made startling gains in the past 20 years. During that period the number of persons covered has gone from 12 million to 123 million. It is estimated that 60% of the aged, needing and wanting health insurance, will have it this year, 75% by 1965, and 90% by 1970. Further, voluntary effort at the community level is rapidly developing and expanding special facilities for the health care of the aged.

Q. Would the bill help the indigent aged with the lowest incomes?

A. No. Despite its enormous cost, the Forand bill would not help the indigent, for the vast majority of them are not eligible for Social Security retirement and survivorship benefits. The indigent receive most of their medical care through welfare programs. Aside from the help they get from private, fraternal, and religious organizations, the indigent of all ages now receive more than 4 billion dollars annually in federal and state aid for medical and other expenses.

Q. Would the Forand bill mean better health care for the aged persons covered?

A. No. It would mean poorer, not better, health care for these people. The medical needs of the aged vary widely and can be met only on a basis of each person's particular problem. The care of the aged cannot be blueprinted in Washington, D. C. It must be tailored in each community to fit the need.

In my opinion political medicine is bad medicine—bad for the individual and for the nation.

Louis M. Orr, M.D.
Orlando, Fla.

ORGANIZATION SECTION

STATEMENT OF DR. CHARLES L. FARRELL BEFORE SUBCOMMITTEE ON ADMINISTRATION OF SOCIAL SECURITY LAWS OF HOUSE WAYS AND MEANS COMMITTEE

November 10, 1959

Mr. Chairman and Members of the Committee:

My name is Charles Farrell. I am a physician from Pawtucket, Rhode Island, where I am engaged in the private practice of medicine as a general practitioner, specializing in gynecology. I appreciate the opportunity to appear before this Committee to present the views of the American Medical Association on several matters in connection with the disability provisions of Title II of the Social Security Act. Although I am a member of the Medical Advisory Committee of the Social Security Administration and have participated in its deliberations for several years, my appearance here today is on behalf of the American Medical Association. I am accompanied by Mr. Paul R. M. Donelan, a member of the Law Division of the Association and a member of our Washington office staff. He will assist me in answering questions which the Committee may have following the presentation of our formal statement.

I should like to address myself to (1) a review of some of the activities of the American Medical Association in this field and its relationship to the disability program; (2) the procurement of medical evidence; (3) a description of the method of operation physicians would prefer to work under in the administration of this program. These points cover the three broad subjects recommended for discussion by Mr. Fred Arner in his communication of October 2 to Mr. James Foristel of our Washington office.

With regard to the present attitude of the medical profession toward this program, I am privileged to inform you that the American Medical Association and its members have accepted their public responsibility by cooperating in every way possible to insure the successful operation of the Social Security disability program which the Congress enacted in 1954. Although the medical profession opposed the legislation, it has, since its enactment, cooperated to the fullest extent when called upon by program officials. Moreover, the American Medical Association has, through the publication of two articles in The Journal *of the American Medical Association* and their subsequent wide distribution, sought to inform physicians as to the scope and objectives of the program, and on the obligations and responsibilities of all physicians in providing information and medical evidence to assist agency determinations of disability.

The A. M. A. has, further, recommended the appointment of committees by every constituent medical association to consult with and render such assistance as they can to state agencies administering the program. It has cooperated with the Division of Disability Operations in the preparation of a special information article by Dr. Roemmich, its medical director, which will appear in The Journal in the near future. It has given permission to the Bureau of Old-Age, Survivors and Disability Insurance to utilize these materials as the Bureau sees fit.

Recently, the Association signed an agreement with the Bureau to co-sponsor a special film project to disseminate more widely and dramatically information about the disability program and responsibilities of physicians under it. Expert technical personnel has been assigned to participate in this endeavor. The underlying theme in all of these efforts has been that of informing physicians that their paramount contribution consists of providing medical evidence as it pertains to one criterion in disability determination; namely, physical and mental impairment. Physicians have been impressed with the fact that they are neither required, nor competent, to make any determination of disability as defined by law.

Finally, the American Medical Association has been privileged to have representatives from its Committee on Medical Rating of Physical Impairment attend meetings of the Medical Advisory Committee of the Social Security Administration to participate in various discussions and to present for solution certain problems which have, at times, required serious study. These activities and efforts testify to the desire of the Association to assure successful and efficient administration of the disability program.

One of the areas of mutual interest and concern to your Committee and to the medical profession is that which involves the procurement of medical evidence. We have given this problem considerable thought and have reviewed various experiences encountered by physicians as well as those of the Division of Disability Operations in arriving at the suggestions which we have to offer. Before doing so, however, I should like to observe that this subject has many ramifications, some of which Dr. George F. Gsell touched upon in his testimony of November 5 to the Committee. Without attempting to occupy too much time in pointing out the various ways in which an applicant may secure medical report forms from his physician, and some of the problems inherent in this procedure, I would briefly like to cite several examples to illustrate the basis for the medical profession's concern with this problem.

First, there is the applicant who has not seen his personal physician for a considerable period of time, perhaps several years. It may be that he or a member of his family merely takes the medical report form to this physician for completion, rather than seeking a new medical evaluation at the time of application. In this case, the physician naturally cannot provide current information or results of recent laboratory tests and findings. He fills out the report on the basis of his past knowledge and care of the applicant. This may not provide sufficient data for the reviewing officer to make a determination and the state agency may be compelled to ask for a consultative examination—for which the consulting physician is reimbursed by BOASI. In such cases, the applicant's physician is frequently criticized at the state level for supplying inadequate data. However, it is not at all unlikely that had he been given an opportunity to personally check the applicant, sufficient data could have been obtained from him. Thus, we perceive a situation which may (*a*) create unwarranted criticism of physicians, (*b*) cause delays in adjudication, and (*c*) authorize payment to a consultant for doing what the original physician could have done. All of this tends to create friction between the medical profession and the agency administering the disability program. The patient may be unable to pay for the necessary laboratory data to insure the probable acceptance of his claim by the state agency.

A second situation arises when the applicant seeks the completion of his medical report form from a physician who has examined the patient recently. In some of these cases a medical reevaluation may be necessary but the applicant does not believe so, since he has recently seen the physician. Again, special data may be required and the process just reviewed occurs. In any event, the physician and his staff must spend considerable time in completing the form in order to supply full and up-to-date information.

In neither of these cases is the physician reimbursed by the state agency and frequently does not charge the patient, despite the amount of work involved. However, in each case, the physicians are aware of the fact that a colleague may be reimbursed by the state agency for performing a consultative examination or obtaining essential laboratory data and for recording the patient's medical history, all of which the original physician is probably able to do.

The third situation may arise when the applicant brings his medical report form to his physician. The physician performs a thorough examination, together with appropriate laboratory and x-ray examinations, takes a complete history and then fills out the form. Here he generally charges the patient only for the medical services he rendered.

The question of reimbursement is one which cuts across several lines in the patient-physician relationship; the desire of the physician to assist his patient without imposing a financial burden on him; the ability of the physician to provide current reports if he realized that he would be reimbursed just as a consultant is; and the conflict which arises in charging a fee for recording in detail the medical reports which the agency requires of the applicant.

This problem is not too dissimilar from one which confronts physicians in the completion of insurance claim forms. As far back as February 12, 1955, an editorial appeared in The Journal *of the American Medical Association* dealing with this problem. At that time, the attention of physicians was directed to the "area of primary interest" involved in the determination as to whether physicians should charge patients for completing medical report forms, or whether such charges should be made to insurance companies. The editorial stated, "If an insurance company makes an inquiry of a physician for the purpose of evaluating a risk at the time of underwriting or for the purpose of reappraisal of a risk, perhaps a charge to the company is justifiable. On the other hand, if the purpose of supplying the information is to assist the insured in collecting a benefit, then the physician might well consider this as part of his service to the patient."

The Social Security Act requires the claimant to furnish such proof of the existence of the alleged disability as may be required. The present policy is to require sufficient medical evidence with the initial claim to show there is a reasonable likelihood that a disability exists. The claimant must supply this at his own expense. If further medical data are needed for a sound determination, the Bureau may authorize its purchase at government expense. This, in our opinion, is a sound approach.

We believe, however, that when additional medical data are needed for a sound determination, such further information should be obtained from the claimant's own physician, if possible, in a similar manner to the way it is now obtained from a "consulting physician." BOASI should be authorized to require the state agency to make arrangements with the medical profession in the respective states that will permit them to purchase these supplementary examinations, laboratory or other tests from such physicians and under such circumstances as to promote further doctor-patient relationships and rapid development of comprehensive information.

Some of the problems that have arisen in the past have probably resulted from the backlog created when this program was expanded from a disability "freeze" to add cash disability benefits. Since this amendment was adopted the time required to process claims has been cut in half—and is now 2½ months. Most cases are now decided on the medical evidence submitted by the claimant as substantiated by hospital and other records. In other cases and in reconsiderations, the increase in the number of consultative examinations has helped to accelerate adjudication of cases.

From years of experience with various governmental programs, the medical profession has reached the conclusion that it can make its most effective contribution where such programs are administered on a decentralized basis. Differences in local customs and conditions require negotiations and arrangements on a state-by-state basis. This method of administration results in a more ready exchange of ideas, better communications, cooperation, and understanding. The accessibility and ease of communication which exist under the Social Security disability program have facilitated the recognition and resolution of problems which might otherwise be neglected or remain unrecognized in the welter of administrative detail and procedure. We urge the continuation of this principle as an aid to the public and to the Congress in assuring the fulfillment of the intent of this legislation.

Our concluding remarks concern the role and relationship of the Office of Vocational Rehabilitation to the disability program. The American Medical Association is fully cognizant of the problems involved in placing people in employment once they have been rehabilitated. We regret, however, that more applicants are not being rehabilitated and that more information is not available as to the reasons why they are not accepted for rehabilitation. We believe that such information is essential to a complete understanding of the problems involved. We hope that this Committee will consider the matter of sufficient importance to recommend the collection and publication of such data.

I wish to thank you again for this opportunity to appear before your Committee on behalf of the American Medical Association to present information concerning our continuing interest in the Social Security disability program. We are grateful for the chance to offer suggestions for possible solutions to the problems which you are inquiring into, and to raise points which may contribute to a clearer understanding of some facets of the disability program.

If you have any questions, Mr. Donelan and I will attempt to answer them.

DALLAS CLINICAL MEETING SCIENTIFIC PROGRAM

The Scientific Program at the Dallas Clinical Meeting received much praise for its outstanding contribution to continuing graduate medical instruction. There were many statements such as the following:

> It was not only the best A. M. A *meeting* I ever attended, it was the best meeting I ever attended anywhere.

> The over-all interest of the visiting doctors to the scientific exhibits and clinical meetings was the most wonderful we have seen. The entire atmosphere was charged with enthusiasm and willingness to see, be shown, and learn

> I have attended all the A. M. A. Clinical Meetings since they were started and have found them so superior that I have discontinued going to the Annual Meeting.

The program was extensive in character, consisting of 269 separate presentations of lectures, symposiums, panel discussions, color television, motion pictures, breakfast conferences, and scientific exhibits. The participants numbered 543 and came from 39 different states as well as the British Isles.

The lectures were especially popular, with overflow audiences most of the time. Adjacent to the lecture hall there were rooms for panel discussions and symposiums which were attended by capacity audiences. Programs in all three rooms were conducted simultaneously and continuously.

Medical motion pictures were correlated with the lectures, the subjects being integrated so that physicians could listen to the lecture and then see the motion picture in an adjacent hall. Large audiences attended most of the film showings.

Color television broadcasts originated at Parkland Memorial Hospital and were carried to the auditorium by closed circuit. Arrangements for the television programs were made with meticulous care and appreciative audiences viewed the presentations.

The Scientific Exhibit on the lower floor of the auditorium contained 120 exhibits, each of which was attended by a competent demonstrator. The hundreds of physicians who watched the demonstrations and asked questions attested to the popularity of this type of presentation.

There were several attractive special features. The special exhibit on fractures, under the chairmanship of Ralph G. Carothers, M.D., Cincinnati, was judged "the most helpful shown" by spectators. The manikin demonstrations on problems of delivery were always popular, the question period sometimes extending far beyond the allotted time. The symposium on sunlight and the skin, presented by the Committee on Cosmetics of the American Medical Association, was very successful, being called by one physician "the most instructive session ever attended." The 10 breakfast conferences on two mornings were attended by capacity audiences, in most instances, and were designated a "must" for future Clinical Meetings. The evening motion picture program was presented for visiting physicians not otherwise occupied and was eminently successful. The Transatlantic Conference with the Glasgow Division of the British Medical Association kept a rapt audience in its seats to the very end. An eminent panel in Dallas, headed by John S. Chapman, M.D., was matched by an equally eminent panel in Glasgow, headed by W. Arthur Mackey, M.B.

Credit for the success of the meeting belongs to the many different persons engaged in the preparation and presentation of the program. Everett C. Fox, M.D., Dallas, was chairman of the local committee on arrangements and gave unstintingly of his time throughout the year. C. D. Bussey, M.D., Dallas, chairman of the scientific program committee, exercised initiative in the preparation of the program and paid minute attention to detail during its presentation. John S. Chapman, M.D., television chairman, and James A. Martin, M.D., scientific exhibit chairman, deserve credit for the work which they did in their respective areas, as does Don G. Harrel, M.D., Dallas, for the manikin demonstrations on problems of delivery. Mr. Millard J. Heath, Dallas, and Mr. C. Lincoln Williston, Austin, Texas, executive assistants of the local committee, were always available. Appreciation is also extended to Smith Kline and French Laboratories, Philadelphia, for sponsorship of the color television program and the Transatlantic Conference.

GOVERNMENT SERVICES

ARMY

Reassignment.—Col. Laurence A. Potter, assistant commandant of the Army Medical Service School, Brooke Army Medical Center, has become deputy chief of the personnel and training division in the office of the surgeon general.

PUBLIC HEALTH SERVICE

Little Strokes.—A new brochure of the Public Health Service stresses the importance of prompt diagnosis of little strokes and indicates that early treatment often prevents more serious strokes. The booklet, "Little Strokes—Hope Through Research," calls attention to such minor and sometimes baffling symptoms of little strokes as thickness of speech, dizziness, or numbness of arm or leg. It warns, however, against attempted diagnosis by the patient or his family and points out the vital importance of immediate medical care. It was prepared by the National Institute of Neurological Diseases and Blindness and is listed as Public Health Service Publication no. 689. Single free copies may be obtained from the National Institute of Neurological Diseases and Blindness, Bethesda 14, Md. Quantity orders cost $7.50 for 100 copies from the Superintendent of Documents, Government Printing Office, Washington 25, D. C.

Recent Appointment.—Dr. Robert E. Olson, head of the biochemistry and nutrition department at the graduate school of public health and lecturer in medicine at the school of medicine, University of Pittsburgh, was appointed to serve a three-year term on the biochemistry training committee of the National Institutes of Health. As a member of the committee, Dr. Olson will review applications for training grants in the field of biochemistry and will provide technical advice to the National Advisory Health Council of the National Institutes of Health and, through the Council, to the surgeon general of the Public Health Service on matters pertaining to research problems of the nation.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Recent Appointment.—Dr. James Watt, director of the National Heart Institute of the Public Health Service, was appointed special assistant for Aging to Secretary Flemming. This post was created as a further recognition of the increased importance of aging as a concern of the department.

FOOD AND DRUG ADMINISTRATION

Cerumen Removers.—Three new products for removing wax from the ears have caused painful injuries and are being voluntarily withdrawn from the market. All three products had previously been cleared by the Food and Drug Administration as being safe for sale without prescription. The injuries, which apparently occur only in sensitive users, were not evident from the clinical studies that preceded marketing. The products involved are (1) Kerid, distributed by Blair Laboratories, New York, (2) Cerulav, distributed by G. F. Harvey Co., Inc., New York, and (3) Cerumenex, distributed by Purdue Frederick Co., New York.

Consumers who have purchased these drugs are warned that their use may result in temporary swelling and soreness of the ear, accompanied by a rash on surrounding areas of the face and neck in some cases. The reported reactions have lasted from 2 to 10 days and have cleared up without permanent injury. About 180 such reactions have been reported. The manufacturers estimated there have been over 1 million users to date. A spokesman for all three firms said, "Notwithstanding the low incidence of the reactions, the manufacturers are withdrawing the products. The companies plan to file another new drug application which would provide for sale of these drugs through medical prescription."

MEDICAL NEWS

CALIFORNIA

Hospital for Dental Patients.—A hospital for dental patients has been opened in Los Angeles. The 80-bed Southern California Dental Hospital specializes in cases where general anesthesia is used. Patients are able to rest in recovery rooms or stay overnight or longer in private rooms with patios, television, radio, etc. Dentists are provided with laboratory and x-ray facilities and hospital conveniences including piped oxygen and nitrous oxide, ultrahighspeed turbine drills, and closed-circuit television. The $1,750,000 three-story unit in the Los Angeles hospital center opened in September.

Meeting of Obstetricians and Gynecologists.—On Feb. 8-12, the 15th annual midwinter clinical assembly in obstetrics and gynecology will be presented in Los Angeles by the Obstetrical and Gynecological Assembly of Southern California. The assembly, arranged particularly for the established specialist, will feature the following guest lecturers: Richard J. Blandau, Ph.D., Seattle; Dr. Louis M. Hellman, Brooklyn; Dr. Herbert E. Schmitz, Chicago; Dr. Jacques Varangot, Paris; and Joseph T. Velardo, Ph.D., New Haven, Conn. A two-day meeting for younger specialists, residents, and those interested in obstetrics and gynecology, the annual forum, will be held Feb. 6 and 7, with the assembly faculty participating. For information on the forum, write Dr. Kenneth F. Morgan, Suite 910, 2010 Wilshire Blvd., Los Angeles 57. Correspondence concerning the assembly should be directed to P. O. Box 57118, Flint Station, Los Angeles 57.

COLORADO

Approve New Construction in Expansion Program.—New construction totaling nearly one million dollars for the University of Colorado Medical Center campus in Denver was approved by the board of regents. The action followed a request by Dr. Robert J. Glaser, vice-president for medical affairs and dean, for authorization to use building mill levy funds to speed two projects which are part of the projected $17,250,000 expansion program. The new structures are a $417,000 addition to Denison Memorial Library and a $515,000 children's day care center for treatment of children suffering from psychiatric illness.

MISSOURI

Dr. Wakefield Comes to Springfield.—Dr. Elmer G. Wakefield, member of the staff of the Mayo Clinic, Rochester, Minn., from 1930 to 1932 and from 1934 to this year, has come to Springfield to carry on the private practice of medicine. He is a fellow of the American College of Physicians and a diplomate of the National Board of Medical Examiners.

Personal.—The new president of the Missouri Division of the American Cancer Society, elected in October, is Dr. John M. T. Schattyn, St. Louis.——Dr. Paul E. Lacy, St. Louis, has been named assistant dean of Washington University School of Medicine, St. Louis, Dean Edward W. Dempsey announced. A member of the medical school staff since 1956, Dr. Lacy is assistant professor of pathology. As assistant dean, he succeeds Dr. John C. Herweg, St. Louis, assistant professor of pediatrics, who had held the administrative position since October, 1952.——The Missouri Hospital Association achievement award for exceptional service to his community, its hospitals and his profession was given to Dr. Archibald E. Spelman, Smithville, during the annual meeting in St. Louis in late October.——Governor Blair recently appointed Dr. Carl M. Peterson, Kansas City, as a member of the board of curators of Lincoln University.——The new medical director of the Research Clinic, Kansas City, is Dr. Frank B. Leitz, Kansas City.

MONTANA

Interim Meeting in Helena.—The 1960 interim session of the Montana Medical Association will be held in Helena on Friday and Saturday, Feb. 26-27. All sessions of the House of Delegates and all of the scientific meetings will be held at the Western Life Insurance Company Building. The first session of the House of Delegates will convene at 8:30 a. m., Friday, Feb. 26. The scientific sessions will convene immediately after the adjournment of the house and will continue until 5:30 p. m. On Friday evening the interim session banquet will be held. A program of entertainment is planned. For information, write the Montana Medical Association, P. O. Box 1692, Billings, Mont.

NEW YORK

Surgical Society Sponsors Lecture.—The Buffalo Surgical Society will sponsor the Roswell Park Lecture on Feb. 9 in honor of Dr. Roswell Park, professor of surgery, University of Buffalo, 1883-

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

1914. The lecturer and recipient of the Roswell Park Medal will be Dr. Herbert A. Smith, professor of surgery emeritus, University of Buffalo. The title of this year's lecture is "Lest We Forget." This will be the 13th lecture. In 1959, Dr. Michael E. DeBakey, Houston, Texas, was the lecturer.

Plan Center for Chronically Ill.—As part of its greater university program of expansion, the University of Rochester Medical Center announced it will build a four-story diagnostic and treatment center for the chronically ill at a cost of $1,317,220. Construction will begin in mid-March with the expectation that the facility will be completed by the spring of 1961. The new center will be a self-contained unit with equipment and specialists on hand. About one-half of the 32,000 square feet available will be devoted to rehabilitation facilities, including areas for physical therapy, occupational therapy, an evaluation clinic, and speech and hearing sections. Activities will be designed to train the handicapped to care for themselves in daily living. The remaining half of the space will be used for complete diagnostic facilities for ambulatory patients and will include a prosthetic clinic. Dr. Robert L. Berg, professor of preventive medicine and community health, will direct the center. The U. S. Department of Health, Education, and Welfare has given preliminary approval to a grant of $334,954 to Strong Memorial Hospital for the center. Other funds to be applied to the project will be $249,000 from Ford Foundation grants totaling 3 million dollars, and $275,000 from a Commonwealth Fund grant totaling $750,000.

New York City

Courses in Radiological Health.—The department of industrial medicine of the New York University–Bellevue Medical Center Post-Graduate Medical School will offer two courses in radiological health starting March, 1960. This program makes available to research institutions, industry, and government facilities for training technical people having responsibilities in the expanding field of radiological protection. The courses are intended for persons already trained in one of the physical, engineering, biological, or medical sciences who require a comprehensive introduction to the new techniques and methods associated with radiological hazard evaluation. The courses are as follows:

Medical and Public Health Control of Ionizing Radiation.—Full time, March 7-18, 1960. Primary emphasis is on the biological effects of radiation and medical control programs. Designed for public health officials, physicians, and others with biological interests.

Radiation Hygiene Measurements.—A four-week intensive course, April 18 through May 13, offering laboratory instruction in surveying, monitoring, and sampling procedures for persons having some acquaintance with nuclear measurement principles.

For information, write the Associate Dean, New York University Post-Graduate Medical School, 550 First Ave., New York 16.

Columbia University Receives Record Gift.—Columbia University on Jan. 3 received a gift of 5 million dollars, the largest single gift ever contributed by a living person to the 205-year-old institution. The donor is alumnus William Black, a resident of New Rochelle, N. Y., president and founder of the Chock Full O'Nuts Corporation and president and founder of the Parkinson's Disease Foundation, with national headquarters at 125 E. 50th St., New York City. Mr. Black's gift will go toward construction of an 18-story medical research building at 168th Street and Fort Washington Avenue, on the grounds of Columbia University's College of Physicians and Surgeons. One of the floors will be devoted to research projects of the Parkinson's Disease Foundation. The foundation, which was endowed by Mr. Black when he founded it, has supported 25 scientific research projects in neurological centers in the United States. It is expected that the new building will be the largest voluntary medical research building in the United States. Its 18 floors will contain more than 200,000 square feet. The structure will be known as "The Jean and William Black Medical Research Building."

Personal.—The appointment of Dr. Reynold C. Merrill to the position of associate director of the research and development laboratories in charge of biological research, Squibb Institute for Medical Research, was announced. He has been serving as Squibb's director of clinical research in the medical division.——Dr. Leonard Greenburgh resigned from his post as commissioner of the New York City Department of Air Pollution Control, effective Jan. 8, to take a position as professor and acting chairman of the department of preventive medicine at the Albert Einstein College of Medicine. Dr. Greenburgh has been commissioner of the Department of Air Pollution Control since the establishment of the agency in November, 1952. He is currently president of the Air Pollution Control Association.——Dr. Barbara Fish was appointed associate professor of clinical psychiatry at New York University College of Medicine and psychiatrist-in-charge of the Children's Service of Bellevue Hospital Center. Prior to this appointment, Dr. Fish was assistant professor of clinical pediatrics, instructor in psychiatry at Cornell University Medical College, and child psychiatrist in the department of pediatrics at New York Hospital.——Dr. Marshall I. Hewitt was named director of clinical research, domestic, of E. R. Squibb & Sons. Dr. Hewitt was editor of professional literature at another pharmaceutical company for two years before joining Squibb as an associate medical director in 1954.

NORTH CAROLINA

Fund for Research Center.—A campaign is being conducted by the medical alumni of Wake Forest College throughout North Carolina and the rest of the nation to aid the school in constructing a $750,000 building to house a major share of its research activities. The building is to be a part of the medical center formed by the North Carolina Baptist Hospital and the Bowman Gray School of Medicine. It will be five stories high with most of the space allocated to research laboratories "which can be adapted to any kind of research activity."

PENNSYLVANIA

Dr. Rogers Named Chairman of Expanded Department.—The University of Pittsburgh School of Medicine received a $400,000 gift from the A. W. Mellon Educational and Charitable Trust. Funds from the gift will be used over an eight-year period to expand the teaching program of the school's department of preventive medicine, starting July 1. Dr. Kenneth D. Rogers, associate professor of maternal and child health at the Pitt Graduate School of Public Health, will become professor and chairman of the department of preventive medicine. Dr. Rogers, who has been a member of the University of Pittsburgh faculty since 1953, listed two main educational objectives of the department as follows: (1) to expand the scope of preventive medicine teaching beyond the traditional areas of water and food sanitation, waste disposal, immunization, public health laws and regulations, and vital statistics, and (2) to demonstrate the application of preventive medicine concepts to students in a clinical setting. The expanded program will include health promotion and protection, early recognition and prompt treatment of diseases, limitation of disability, and the concept of positive rehabilitation when disability cannot be prevented.

RHODE ISLAND

Society Elects President in Absentia.—For the first time in its 113-year history the Providence Medical Association elected a president in absentia when it named Dr. Irving A. Beck, Providence internist, at its annual meeting Jan. 4. Dr. Beck is currently in Israel as a member of an exchange team of physicians from Miriam Hospital conducting medical educational programs in that country. Other officers elected by the local association were: Drs. Frank D. Fratantuono, vice-president; Dr. William A. Reid, secretary; Dr. Frank I. Matteo, treasurer; Dr. Francesco Ronchese, trustee of the medical library; and Drs. J. Merrill Gibson, Harry E. Darrah, Francis W. Nevitt, and William J. MacDonald, new members of the executive committee for three-year terms each.

VIRGINIA

Ground Broken for New Hospital.—Ground-breaking ceremonies for Alexandria's new hospital took place on Monday, Dec. 7. On hand to turn the first shovelful of earth was Virginia's chief executive, Governor J. Lindsay Almond. The erection of the new $3,650,000 hospital is being financed by the federal Hill-Burton program (55% of the cost) and by an extensive fund-raising campaign which has been going on for over two years. Presently, over 4,000 families and businesses have contributed more than $915,000 for the project. The hospital fund-raising campaign will continue until the required funds have been forthcoming. Meanwhile, in order to avoid further delay in constructing the new hospital, several local financial institutions are providing the necessary funds, which will be repaid by future contributions. Governor Almond spoke at the 26-acre site of the 150-bed hospital at Seminary Road and North Howard Street.

Lecture Series on Mental Hygiene.—The Lynchburg Training School and Hospital of the Virginia Department of Mental Hygiene and Hospitals announced that it will present a lecture series throughout the year. The series will be formally opened by Dr. Hiram W. Davis, Richmond, commissioner, department of mental hygiene and hospitals, who will introduce the first speaker on Feb. 3. On that day Dr. David C. Wilson, professor of psychiatry at the University of Virginia, will discuss at 10 a. m. "The Psychological Reaction to Organic Defects." Other lectures are scheduled as follows:

Feb. 25 and 26.—Dr. Robert A. Senescu, Richmond, "Emotional Illness as a Failure in Adaptation."
March 14.—Dr. Ian P. Stevenson, Charlottesville, "Psychotherapy Based on Learning Theory."
March 24.—Dr. Lever F. Stewart, Charlottesville, "Myasthenia Gravis" and "Toxic Diseases and Deficiency States Affecting the Central Nervous System."
April 18.—(Topic to be announced) As professor in residence, Miss Agnes Lucas, R.N., M.S., Roanoke.
May 26 and 28.—As professor in residence, Dr. Howard W. Potter, Letchworth Village, N. Y.
June 3.—Dr. Patrick H. Drewry Jr., Richmond, "Deprivation and Anti-Social Behavior."
June 6 and 8.—A three-day institute devoted to problems of special education in mental retardation.
June (date to be announced).—Dr. Weir M. Tucker, Richmond, "Schizophrenia."
October (date to be announced).—Dr. James B. Funkhouser, Richmond, "Electroencephalography."

WISCONSIN

Plastic Surgery Group Organized.—The organization of the Wisconsin Society of Plastic Surgery was announced. The following officers were elected: president, Dr. Christopher R. Dix, vice-president, Dr. William H. Frackelton, secretary-treasurer, Dr. Jack Teasley, of Milwaukee; and board of directors, Dr. Volney B. Hyslop, Milwaukee, Dr. Frank D. Bernard, Madison, and Dr. Paul Natvig, Milwaukee.

Personal.—James F. Crow, Ph.D., chairman of the department of medical genetics, University of Wisconsin Medical Center, Madison, was elected president of the Genetics Society of America. Newton E. Morton, Ph.D., assistant professor of the same department, was appointed by the board of directors of the American Society of Human Genetics to represent them on the program committee for the second International Congress of Human Genetics to be held in Rome, Italy, in 1961.——Dr. Kenneth E. Lemmer, professor of surgery, University of Wisconsin Medical School, Madison, was elected to membership in the International Society of Surgery, a worldwide group with its headquarters in Brussels, Belgium. Election to the society is on the basis of research accomplishments.

GENERAL

English Surgeon Speaks at Meeting.—Mr. Guy Pulvertaft, F.R.C.S., of Derby, England, was the guest speaker at the 15th annual meeting of the American Society for Surgery of the Hand in Chicago, Jan. 22-23. Mr. Pulvertaft presented a paper, "Tendon Grafting for Division of Flexor Profundus," and also led a discussion and question-and-answer period covering other papers on tendon surgery.

Change Dates for Orthopedic Meeting.—There has been a change in dates scheduled for the 1960 meeting of the Mid-Central States Orthopaedic Society. The meeting will be held Friday, April 8, and one-half day on Saturday, April 9, in Wichita, Kan. This change has shortened the meeting by one day. Registration will begin on Friday morning, April 8. For information, write Dr. H. O. Marsh, 3244 E. Douglas, Wichita 8, Kan., Secretary.

Southeastern Meeting of Plastic Surgeons.—The annual meeting of the Southeastern Society of Plastic and Reconstructive. Surgeons will be held Feb. 11-14 in the Tides Hotel, St. Petersburg, Fla. Officers of the society are: president, Dr. Robert A. Greer Ricketson, Nashville, Tenn.; president-elect, Dr. Robert F. Hagerty, Charleston, S. C.; vice-president; Dr. Francis A. Marzoni, Birmingham, Ala.; and secretary, Dr. Charles E. Horton, Norfolk, Va. For information, write Dr. Grover W. Austin, 666 6th St., South, St. Petersburg, Fla.

Pharmaceutical Group Establishes Law Division.—A Legal Division has been established by the American Pharmaceutical Association as an integral part of the association headquarters staff in Washington, D. C., and pharmacist-lawyer Raymond J. Dauphinais has been appointed director of the new division. Mr. Dauphinais, who will assume his new position on Feb. 1, was the American Pharmaceutical Manufacturers' Association's fellow in food and drug law during 1955-1956. He has served as assistant professor of pharmacy at the University of Connecticut School of Pharmacy since February, 1957.

Meeting of Catholic Psychiatrists.—The 11th annual meeting of the Guild of Catholic Psychiatrists will be held in St. Louis Feb 8-10 at St. Louis University. The program will include the following seminar subjects:

Psychiatric Aspects of Annulment (two sessions).
Mental Health Orientation for Religious.
The Role of the Chaplain in a Mental Hospital.
Psychiatry and Moral Theology.
Psychiatric Aspects of Obscene Literature.

For information, write Dr. William B. Lytton, 7301 St. Charles Rock Road, St. Louis 14, General Chairman.

Change Date on Aviation Hearing.—The informal public hearing on FAA Draft Release 59-2 "Certification Procedures; Class III Medical Examinations and Certificates by Medical Examiners," originally scheduled for Jan. 14, has been postponed to Feb. 11, the Federal Aviation Agency announced. The hearing will take place 10 a. m. at FAA Headquarters, 1711 New York Ave., N. W., Washington, D. C., and will provide participants with an opportunity to present their views on Draft Proposal 59-2. This draft release recommends that applicants for student and private pilots secure their medical examinations from designated medical examiners. The proposal had previously been published in the Federal Register and circulated to interested persons for written comment.

Protestant Hospital Meeting.—The 39th annual convention of the American Protestant Hospital Association will be held Feb. 19, with a meeting of Protestant Denominational Groups to be held Feb. 16-18, at the Deshler Hilton Hotel, Columbus, Ohio, under the presidency of Mr. Edwin B. Peel, administrator, Georgia Baptist Hospital, Atlanta. The following papers are scheduled for presentation on the hospital program:

The National Picture, Robert M. Cunningham Jr., Chicago.
The Nursing Dilemma, Eleanor C. Lambertsen, Chicago.
The Christian Approach to Solving the Problem, Bolton Boone, Dallas.
The Impact of Church Hospitals on Health Services, Frank S. Groner, Memphis.
Report on Future Plans of the American Protestant Hospital Association, Rev. Carl C. Rasche, St. Louis.

A theme, "Personnel Practices and Their Effect on Patient Care and Hospital Costs," will be moderated by Dr. Frank Bradley, president-elect of the association and director, Barnes Hospital, St. Louis. Mr. Peel will preside at a fellowship dinner the evening of Feb. 18. For information, write the American Protestant Hospital, 840 N. Lake Shore Dr., Chicago 11.

Award for Paper on Rehabilitation.—The third Bernard M. Baruch Essay Award, sponsored by the American Congress of Physical Medicine and Rehabilitation, was announced. Any subject of interest or pertaining to physical medicine and rehabilitation may be submitted. Manuscripts must be in the office of the American Congress of Physical Medicine and Rehabilitation, 30 N. Michigan Ave., Chicago 2, not later than March 1. Contributions will be accepted from medical students only. The American Congress of Physical Medicine and Rehabilitation shall have the exclusive right to publish the winning essay in its official journal, the *Archives of Physical Medicine and Rehabilitation*. Manuscripts must not exceed 3,000 words, and the number of words should be stated on the title page. An original and one carbon copy of the manuscript must be submitted. The essay must not have been published previously. The winner shall receive a cash award of $100. All manuscripts will be returned as soon as possible after the winner is announced. The winning manuscript becomes the exclusive property of the congress. The American Congress of Physical Medicine and Rehabilitation reserves the right to make no award if, in the judgment of the Essay Award Committee, no contribution is acceptable. Announcement of the winner will be made at the annual meeting.

Report on Hospital Admissions.—Statisticians of the Metropolitan Life Insurance Company report that more men than women at ages 60 and over go to the hospital, but the men stay shorter time than the women. Experience among Metropolitan's personnel indicates that the hospital admission rates in 1957 and 1958 averaged 156 per 1,000 annually for men and 98 per 1,000 for women. However, the average stay was 16.8 days for men, and 27.8 days for women. The group under study, all aged 60 or over, included office and field personnel at work, on disability, or retired. These persons are protected under a hospitalization insurance program. The yearly hospitalization rate among males rose from 159 per 1,000 at ages 60-64 to 185 per 1,000 at ages 75 and over. In each age group, more men were hospitalized for nonsurgical than surgical conditions. The two types of cases were about even for women. The duration of hospitalization per case increased steadily with advance in age among both men and women, and for surgical as well as for nonsurgical conditions. Among males, the average stay per case for all causes combined increased from 13.3 days at ages 60-64 to 24.6 days at ages 75 and over. Among the women, the average rose correspondingly from 16.3 to 37.5 days. Among the males, abdominal and urologic operations accounted for nearly three-fifths of the surgical cases. Heart disease accounted for one-third of the nonsurgical cases. Ranking next in order of frequency were digestive disorders, respiratory conditions, circulatory conditions other than heart, and diseases of the central nervous system. In general, the pattern of hospitalization for women resembled that for men, with abdominal operations the leading type of surgical condition and heart disease the most frequent cause of hospitalization for nonsurgical condition.

Regional Meeting of Physicians.—The American College of Physicians will hold a regional meeting for Louisiana and Mississippi at the Veterans Administration Hospital Auditorium and the Tulane University School of Medicine Auditorium, New Orleans, Feb. 12-13. The following papers will include invited authors:

Idiopathic Hemachromatosis—Report of Ten Cases, Dr. John P. Muhleisen and Dr. John N. Bickers, New Orleans.

Genetic Predisposition to Pernicious Anemia as Studied by Radio-active Technic, Dr. Patricia McIntyre, Shreveport, La.

Differentiation of Leukemoid Reaction from Leukemia, Dr. Warren N. A. Bell, Jackson, Miss.

Myasthenia Gravis in Pregnancy—Case Presentation by Dr. Dan E. Russell, Shreveport, La.

A Clinico-Pathologic Study of the Nephrotic Syndrome by Use of the Renal Biopsy, Drs. Robert R. Burch, Maurice A. Pearl, and William H. Sternberg, New Orleans.

Experimental Studies Concerning the Pathophysiology of Strangulated Intestinal Obstruction, Dr. William O. Barnett, Jackson, Miss.

Unusual Cases of Hyperparathyroidism, Drs. Joseph F. Dingman, Maurice A. Pearl, and William Sternberg, New Orleans.

The Varied Clinical Picture in Cushing's Disease, Dr. Herbert G. Langford, Jackson, Miss.

At the banquet Feb. 12, 8 p. m., at the Roosevelt Hotel, Dr. Irving S. Wright, New York City, regent of the college, will present "The Role of the American College of Physicians in Internal Medicine." Governor for the college for Louisiana is Dr. Marion D. Hargrove, Shreveport, and for Mississippi, Dr. Laurance J. Clark Sr., Vicksburg. For reservations, write Dr. John J. Archinard Jr., 3503 Prytania St., New Orleans 15.

CANADA

Appoint Ophthalmic Research Director.—Dr. P. K. Basu was appointed the Stapells Director of Ophthalmic Research in the University of Toronto, made possible by Mr. H. G. Stapells, Q. C., of Toronto. The object of the Stapells Fund is to further ophthalmic research work in the department of ophthalmology in the University of Toronto. Dr. Basu will direct and coordinate the ophthalmic research in the department and carry on active research himself on diseases of the eye.

FOREIGN

Congress on Cancer in Australia.—A cancer congress will be conducted by the Anti-Cancer Council of Victoria at the University of Melbourne, Australia, Aug. 22-25. The congress will consist of five plenary sessions and six sectional meetings in which carcinogenesis, cancer in the community, cancer of the lung, leukemia, and cancer of the skin will be considered. Visiting participants will come from the United Kingdom, Israel, the United States, New Zealand, and Japan. An exhibition of cancer pathology, research, and technical aid to diagnosis will be on view throughout the congress. A cancer film program will be conducted daily. For information, write the Honorary Secretary, Victoria Cancer Congress, % Anti-Cancer Council of Victoria, 410 Albert Street, East Melbourne, Victoria, Australia.

German Physicians to Meet During World Assembly.—The German Medical Association, host of the 14th general assembly of the World Medical Association scheduled to convene in West Berlin Sept. 15-22, has extended an invitation to all the physicians to attend. The Bundesarztekammer (German Medical Association) will convene its 1960 annual meeting concurrently with the convening of the general assembly. This is the first time that a host medical association to the World Medical Association has scheduled its own annual meeting in conjunction with the meeting of the world association. The two associations will meet jointly in their opening and closing plenary sessions. All activities including the postgraduate teaching film program, exhibits, and scientific sessions will be held in one building to enable doctors to attend the various sessions associated with each meeting which are of special interest to them. Information including programs and schedules will be available about March 1 at the Headquarters Secretariat, World Medical Association, 10 Columbus Circle, New York 19.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for filing application was January 10. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Internal Medicine: *Oral.* San Francisco, March 30-April 1; New York City, Nov. 14-17. Closing date for filing application is Jan. 2 and July 1. *Written.* Oct. 17. Closing date for filing application is May 1. *Oral. Gastroenterology.* Philadelphia, March 11-12. Final date for filing application was January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. St. Louis, April 10-12. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part II, Oral and Clinical.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* Jan. 23, 1961. Deadline for filing applications is July 1. *Oral.* San Francisco, May 9-13; Chicago, Oct. 3-7. Sec., Dr. Merrill J. King, Box 236 Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral*, Chicago, Oct. 3-7. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Memphis, April 21-23. Final date for filing application is March 7. *Examination in Forensic Pathology.* Memphis, April 22. Final date for filing application is March 7. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. Final date for filing application was January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: San Francisco, March 14-15; New York, New York, Dec. 12-13. *Child Psychiatry.* Chicago, April 25-26. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

American Board of Radiology: *Examination.* Cincinnati, Spring 1960. Deadline for filing applications was Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Oral Examinations (Part II):* New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Feb. 12. Final date for filing application was Dec. 1. *Oral.* May 1960. Final date for filing application was Dec. 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Abraham, Dallas Edward Ⓜ Louisville, Ky.; Hospital College of Medicine, Louisville, 1906; served in France during World War I; died in St. Joseph Infirmary Oct. 22, aged 78.

Baum, Frank Joseph, McAlester, Okla.; Arkansas Industrial Medical Department, Little Rock, 1891; died Oct. 8, aged 89.

Behrend, Ralph Arthur, Santa Barbara, Calif.; Yale University School of Medicine, New Haven, Conn., 1931; at one time associated with the city health department in Long Beach; died Oct. 14, aged 54.

Bird, Jacob Wheeler Ⓜ Sandy Spring, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1907; member of the House of Delegates of the American Medical Association 1948-1951; past-president and past-vice-president of the Medical and Chirurgical Faculty of the State of Maryland; served on the Council on Medical Care of the State Board of Health; served on the gubernatorial commission which led to the establishment of the Maryland State Welfare Department; in July a community celebration was held honoring him for fifty years of medical practice; a founder of Montgomery County General Hospital; died near Huntsville, Ala., Oct. 25, aged 74.

Blecher, John F., Middletown, Pa.; Illinois Medical College, Chicago, 1903; died in Harrisburg Oct. 20, aged 90.

Bower, Charles Franklin Ⓜ Long Beach, Calif.; George Washington University School of Medicine, Washington, D. C., 1907; served on the staffs of Long Beach Community, Seaside Memorial, and St. Mary's hospitals; died in Crescent City, Oct. 25, aged 90.

Bradford, Albert William, Lacon, Ill.; College of Physicians and Surgeons of Chicago, 1895; veteran of World War I; served on the board of health; at one time president of the First National Bank of Lacon; died in the Proctor Community Hospital, Peoria, Oct. 20, aged 87.

Brown, Dewees Englert Ⓜ Donora, Pa.; University of Pittsburgh School of Medicine, 1931; member of the Industrial Medical Association; associated with the Charleroi–Monessen Hospital in Charleroi; died in Mary Fletcher Hospital, Burlington, Vt., Oct. 19, aged 61.

Bruce, Jerald J., Placida, Fla.; University of Nebraska College of Medicine, Omaha, 1922; veteran of World War I; died in Venice Oct. 13, aged 63.

Burch, Lucius Edward Ⓜ Nashville, Tenn.; born in Nashville Dec. 10, 1874; Vanderbilt University School of Medicine, Nashville, 1896; specialist certified by the American Board of Obstetrics and Gynecology; member of the Southern Surgical Association, of which he was past-president, and the Central Association of Obstetricians and Gynecologists; fellow and formerly member of the board of governors of the American College of Surgeons; in 1921 vice-chairman of the Section on Obstetrics and Gynecology and Abdominal Surgery and in 1924 member of the House of Delegates of the American Medical Association; past-president of the Middle Tennessee Medical Society, Nashville Academy of Medicine, and the Vanderbilt Athletic Association; professor emeritus of obstetrics and gynecology and life member of the board of trustees at his alma mater, where he joined the faculty as professor of gynecology in 1904 and served as dean from 1914 to 1925; veteran of World War I; for many years senior obstetrician and gynecologist, Vanderbilt University Hospital; gynecologist at Nashville General Hospital and St. Thomas Hospital; chief surgeon for the Tennessee Central Railroad; collaborator, Pack-Livingston book, "Treatment of Cancer"; served as a member of the advisory editorial board, *American Journal of Obstetrics and Gynecology;* died Oct. 15, aged 84.

Campbell, Francis Mervyn Ⓜ Walla Walla, Wash.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1905; died in Seattle Oct. 30, aged 74.

Chitwood, Edmund Madison Ⓜ Wytheville, Va.; Baltimore Medical College, 1912; member of the American Academy of General Practice; for many years medical examiner for Wythe County; served as surgeon for Norfolk and Western Railway; died Oct. 22, aged 70.

Cope, Thomas Appleton Jr. Ⓜ West Chester, Pa.; born in Philadelphia April 17, 1908; University of Pennsylvania School of Medicine, Philadelphia, 1934; interned at the Germantown Dispensary and Hospital, Philadelphia; specialist certified by the American Board of Pathology; member of the College of American Pathologists; founding fellow of the American Society of Clinical Pathologists; served on the faculty of his alma mater; at various times director of the clinical pathological laboratory at Chestnut Hill Hospital in Philadelphia,

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Ⓜ Indicates Member of the American Medical Association.

Binghamton (N. Y.) City Hospital, and the Nesbitt Memorial Hospital in Kingston; director of the clinical pathological laboratory at Memorial Hospital; died in the Abington (Pa.) Memorial Hospital Oct. 30, aged 51.

Cords, Charles Hillier Ⓜ Rudd, Iowa; State University of Iowa College of Medicine, Iowa City, 1920; died in Eastman, Wis., Oct. 17, aged 66.

Corrigan, Sylvester Edward Ⓜ Billings, Mont.; Harvard Medical School, Boston, 1928; served with the Bureau of Indian Affairs and the U. S. Public Health Service; died in the U. S. Public Health Service Hospital, Seattle, Oct. 20, aged 57.

Davison, Owen Clarence Ⓜ Bethel, Ohio; Miami Medical College, Cincinnati, 1904; died in the Bethesda Hospital in Cincinnati Sept. 19, aged 78

Dozier, Willoughby Jr., Nashville, Tenn.; University of Tennessee College of Medicine, Memphis, 1887; died in the Davidson County Hospital Sept. 17, aged 92.

Edgerton, Merle Marion Ⓜ Coalinga, Calif.; University of Southern California School of Medicine, Los Angeles, 1951; interned at Santa Fe Coast Lines Hospital in Los Angeles; served a residency at Kern General Hospital in Bakersfield; died in Canyon, Mont., Aug. 17, aged 48.

Fischl, Ludwig, Margaretville, N. Y.; Medizinische Fakultät der Universität, Wien, Austria, 1920; died in Sacramento, Calif., Sept. 19, aged 65.

Fleming, Thomas Nicholas Ⓜ St. Cloud, Minn.; Creighton University School of Medicine, Omaha, 1913; served as superintendent of schools in Lyon, Neb., and principal of Omaha High School; died in Albany Aug. 24, aged 79.

Fulbright, James Harvey Ⓜ Springfield, Mo.; Kentucky School of Medicine, Louisville, 1890; fellow of the American College of Surgeons; past-president of the Missouri State Medical Association; past-president of the old St. John's Hospital staff; died in St. John's Hospital Oct. 18, aged 91.

Furbeck, George Nelson Ⓜ San Antonio, Texas; Universidad Nacional Autonoma de Mexico Facultad de Medicina, Mexico, D.F., 1932; fellow of the American Public Health Association; interned at the General Hospital in Mexico City, and the Charity Hospital in New Orleans; specialist certified by the American Board of Preventive Medicine; associated with the San Antonio State Hospital; veteran of World War II; held the Bronze Star with cluster and Purple Heart; died Oct. 22, aged 55.

George, Melbourne E. W. Ⓜ Verona, N. J.; Jefferson Medical College of Philadelphia, 1926; for many years compensation physician for the Travelers Insurance Company in Newark; died in the Mountainside Hospital in Montclair Oct. 19, aged 60.

Glenn, Bernard Hamlin Ⓜ Fowlerville, Mich.; University of Michigan Medical School, Ann Arbor, 1908; in September, 1958, the Michigan State Medical Society presented him with an award for fifty years of practice; died Sept. 21, aged 77.

Green, Sara Elizabeth Ⓜ Miami, Fla.; University of Buffalo School of Medicine, 1906; died in Elmira, N. Y., Oct. 18, aged 91.

Healy, Thomas C. L. Ⓜ Merchantville, N. J.; Georgetown University School of Medicine, Washington, D. C., 1931; interned at the Baltimore City Hospitals; fellow of the American College of Physicians; served as a medical examiner for the Camden (N. J.) Veterans Administration Department of Medicine and Surgery; died Oct. 18, aged 63.

Hill, Stephen Mortimer Ⓜ Vernon, N. Y.; University of Buffalo School of Medicine, 1905; died in Oneida Aug. 25, aged 83.

Hinshaw, Horace Dean Ⓜ La Porte, Ind.; Indiana University School of Medicine, Indianapolis, 1955; interned at the Indiana University Medical Center in Indianapolis; city health officer; died in the Robert Long Hospital, Indianapolis Sept. 16, aged 30.

Hoffman, Wilbur Emory Ⓜ Charleston, W. Va.; born in Keyser, June 24, 1900; Medical College of Virginia, Richmond, 1928; specialist certified by the American Board of Obstetrics and Gynecology; member of the Southeastern Surgical Congress; life member of the American Committee of Maternal Welfare; fellow of the American College of Surgeons; past-president of the West Virginia Obstetrical and Gynecological Society; for many years associated with the Charleston General Hospital; served as consultant in obstetrics at the Herbert J. Thomas Memorial Hospital in South Charleston; died in Charleston General Hospital Oct. 22, aged 59.

Hoyne, Andrew H. Ⓜ Salem, S. D.; Sioux City (Iowa) College of Medicine, 1906; in 1958 was named "General Practitioner of the Year" by the state medical association; died Oct. 15, aged 82.

Jenks, Ralph William, Greenville, Texas; Baylor University College of Medicine, Dallas, 1922; retired director of the Greenville–Hunt County Health Unit; died Oct. 21, aged 65.

Johnson, Rudolph Eugene Ⓜ Norfolk, Neb.; University of Nebraska College of Medicine, Omaha, 1918; member of the American Trudeau Society; served on the school board in Wausa; on the staff of the Norfolk State Hospital; died Oct. 14, aged 67.

Jones, Edmund Dennis Ⓜ Beaumont, Texas; Baylor University College of Medicine, Dallas, 1935; member of the American Academy of General Practice; veteran of World War II; one of the founders of the Texas Academy of General Practitioners; associated with the St. Therese and Hotel Dieu hospitals, and the Baptist Hospital of Southeast Texas, where he died Oct. 23, aged 54.

Lenoci, Ralph Joseph Ⓜ Bridgeport, Conn.; Hahnemann Medical College and Hospital of Philadelphia, 1940; interned at Bridgeport Hospital; formerly resident at the Quincy (Mass.) City Hospital and the Boston City Hospital; during World War II served as a flight surgeon with the Eighth Air Force in England; won six battle stars and the *Presidential unit citation*; on the staff of the Bridgeport Hospital; died in St. Vincent's Hospital Oct. 19, aged 45.

Leonard, Watson W. Ⓜ Tellico Plains, Tenn.; Chattanooga (Tenn.) Medical College, 1900; once served as mayor; died in Sweetwater Oct. 16, aged 83.

Lindner, Eaton George Ⓜ Ocala, Fla.; Miami Medical College, Cincinnati, 1904; also a druggist; for many years city and county health officer; served as physician for the Seaboard Air Line Railroad and the Atlantic Coast Line; on the staff of the Munroe Memorial Hospital, where he died Oct. 20, aged 79.

Locker, George E. Ⓜ Iantha, Mo.; Beaumont Hospital Medical College, St. Louis, 1895; veteran of World War I; also a registered pharmacist; died in the Barton County Memorial Hospital, Lamar, Oct. 19, aged 88.

Lyons, Horace Raymond Ⓜ Tryon, N. C.; Northwestern University Medical School, Chicago, 1916; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; at one time practiced in Chicago, where he was on the staff of St. Luke's Hospital; at one time associated with the Mayo Foundation, Graduate School, University of Minnesota, and the Mayo Clinic, Rochester, Minn.; died Oct. 26, aged 68.

McGuire, John Joseph Ⓜ San Francisco; St. Louis University School of Medicine, 1925; for many years physician for the city fire department; veteran of World War I; served on the staffs of the St. Joseph's and St. Mary's hospitals; died Oct. 26, aged 67.

Manasse, Max Ⓜ Brooklyn; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1912; died Sept. 19, aged 78.

Miller, Albert Hersey Ⓜ Providence, R. I.; born in Lewiston, Maine, April 3, 1873; College of Physicians and Surgeons, New York City, 1898; chairman of the Section on Miscellaneous Topics of the American Medical Association 1932-1933 and 1933-1934, and in 1920 member of its House of Delegates; member of the American Society of Anesthesiologists; past-president of the Providence Medical Association, Rhode Island Medical Society, and the Eastern Society of Anesthetists; in 1932 received the silver cup from the International Anesthesia Research Society in recognition of his achievements; associated with the Truesdale Hospital in Fall River, Mass., South County Hospital in Wakefield, R. I., Memorial Hospital in Pawtucket, Miriam Hospital, St. Joseph's Hospital, Rhode Island Hospital, Jane Brown Hospital, Butler Hospital, and Providence Lying-In Hospital; formerly editor of the *Rhode Island Medical Journal* which dedicated its September issue to him; died in the Rhode Island Hospital Oct. 31, aged 86.

Nagel, Lester R. Ⓜ Arcadia, Calif.; University of Colorado School of Medicine, Denver, 1949; interned at the U. S. Marine Hospital in Boston; served a residency at the U. S. Public Health Service Hospital in Baltimore; associated with the U. S. Public Health Service; specialist certified by the American Board of Pathology; member of the College of American Pathologists; on the staff of the Veterans Administration Hospital, where he died Oct. 14, aged 39.

Padfield, Robert Elmer Ⓜ Noel, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1911; for many years practiced in Wichita, Kan., where he was honorary life member of the staff of St. Joseph Hospital; died Oct. 27, aged 74.

Parker, George M. Ⓜ Carnesville, Ga.; Southern Medical College, Atlanta, 1894; died in the Piedmont Hospital, Atlanta, Oct. 15, aged 92.

Parmacek, Louis Ⓜ Elgin, Ill.; University of Illinois College of Medicine, Chicago, 1928; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; veteran of World War II; formerly chief pathologist at Sherman Hospital; chief pathologist at St. Joseph's Hospital, where he died Nov. 2, aged 55.

Parmelee, Olin Earl Ⓜ Lambertville, Mich.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; died Oct. 21, aged 85.

Patterson, Bertha Elizabeth Schenck Stecker McDavitt Ⓜ Fort Worth, Texas; State University of Iowa College of Medicine, Iowa City, 1907; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; for many years practiced in Temple, where she was associated with the Scott and White Hospital; died Oct. 23, aged 82.

Quire, Frank Edward, Lynnville, Iowa; Rush Medical College, Chicago, 1892; died in Omaha, Neb., Oct. 1, aged 91.

Ratcliff, Marion DeKalb, Auburn, Miss.; Memphis (Tenn.) Hospital Medical College, 1906; died Oct. 26, aged 85.

Robinson, James Ernest, Temple, Texas; Memphis (Tenn.) Hospital Medical College, 1902; fellow of the American College of Physicians; served on the staff of the King's Daughters Hospital; died Oct. 25, aged 81.

Robinsteen, Carl Howard ⓜ Pittsburgh; Hahnemann Medical College and Hospital of Philadelphia, 1908; for many years chief of orthopedic surgery at Shadyside Hospital; died in Charlottesville, Va., Oct. 13, aged 75.

Rote, William Henry ⓜ Williamsport, Pa.; Jefferson Medical College of Philadelphia, 1890; died Oct. 25, aged 95.

Simonton, Thomas Grier ⓜ Pittsburgh; University of Pennsylvania Department of Medicine, Philadelphia, 1895; for many years on the faculty of the University of Pittsburgh School of Medicine, where his portrait was hung during Alumni Day in 1953; past-president of the Pittsburgh Academy of Medicine and the Medical Society of the State of Pennsylvania; on the emeritus staff, St. Francis General Hospital and Rehabilitation Institute; died in St. Francis General Hospital Oct. 19, aged 89.

Simpson, John Clifton, Hamburg, Ark.; Vanderbilt University School of Medicine, Nashville, Tenn., 1914; veteran of World War I; died Oct. 18, aged 67.

Swartwood, Francis Marion, Lincoln, Neb.; Lincoln Medical College of Cotner University, 1915; served on the staffs of the Lincoln State Hospital and the Veterans Administration Hospital, where he died Oct. 14, aged 68.

Swisher, Thomas Justin, Los Angeles; Rush Medical College, Chicago, 1903; formerly practiced in Rawlins, Wyo.; died in the Good Samaritan Hospital Oct. 21, aged 87.

Them, Albert Harrison Jr. ⓜ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1941; veteran of World War II; on the staffs of the Hahnemann, Nazareth, and Frankford hospitals; died Oct. 14, aged 45.

Thomssen, Herbert William, Utica, N. Y.; Jefferson Medical College of Philadelphia, 1905; served as examiner for the Metropolitan Life Insurance Company; formerly practiced in Remsen; died Oct. 13, aged 76.

Thurmon, Francis Mozart ⓜ Boston; Harvard Medical School, Boston, 1926; an examiner for the state division of industrial accidents; on the faculty of Tufts University School of Medicine; specialist certified by the American Board of Dermatology; certified by the National Board of Medical Examiners; fellow of the American Academy of Dermatology and Syphilology; past-president, vice-president, and secretary of the New England Dermatological Society; on the staff of the New England Medical Center; died Oct. 19, aged 60.

Triarsi, Anthony Joseph ⓜ Elizabeth, N. J.; Georgetown University School of Medicine, Washington, D. C., 1934; veteran of World War II; for many years physician for the board of health; on the staffs of St. Elizabeth Hospital, Elizabeth General Hospital, and the Alexian Brothers Hospital, where he died Oct. 30, aged 53.

Undine, Clyde Albert, Minneapolis; University of Nebraska College of Medicine, Omaha, 1916; veteran of World War I; died in St. Barnabas Hospital Aug. 20, aged 73.

Vartanian, Mardiros Bedros, Lawrence, Mass.; University of Illinois College of Medicine, Chicago, 1916; on the staffs of the Bon Secours Hospital, Methuen, and the Clover Hill Hospital; died in the Baker Memorial Hospital, Boston, Oct. 20, aged 71.

Verneuil, Julius Louis ⓜ Collinsville, Ill.; St. Louis University School of Medicine, 1929; member of the American Academy of General Practice; veteran of World War II; on the staff of the St. Mary's Hospital in East St. Louis; died Oct. 25, aged 54.

Walfred, Karl Anderson ⓜ St. Cloud, Minn.; University of Minnesota Medical School, Minneapolis, 1923; member of the American Academy of General Practice; veteran of World War I; county coroner; member and past-president of the staff of St. Cloud Hospital, where he died Oct. 22, aged 69.

Wells, Walker Marshall ⓜ Selma, Calif.; Stanford University School of Medicine, San Francisco, 1937; interned at the San Francisco Hospital, where he served a residency; died Sept. 23, aged 56.

Wheeler, Fred E., Waterville, Maine; Medical School of Maine, Portland, 1901; served in France during World War I; a courtesy member of the Thayer Hospital medical staff; member of the staff of Sisters' Hospital, where he died Oct. 25, aged 87.

Wilkiemeyer, Frederick Joseph, San Jose, Calif.; Harvard Medical School, Boston, 1909; died in Notre Dame Hospital, San Francisco, Aug. 27, aged 80.

Witten, Jack Walter, North Tazewell, Va.; Medical College of Virginia, Richmond, 1905; served overseas during World War I; voted "Alumnus of the Year" by the Medical College of Virginia and received the Algernon Sidney Sullivan Award from Virginia Military Institute; formerly member of the Virginia General Assembly; in 1953 bestowed the Master of Humane Letters by his alma mater; died Oct. 30, aged 79.

FOREIGN LETTERS

BRAZIL

Promazine for Psychoses.—Dr. H. M. de Carvalho and co-workers, of the University of São Paulo, treated 31 psychotic and neurotic patients, most of whom were schizophrenic, with large doses of promazine. This drug is useful chiefly in the treatment of conditions associated with delusions, disturbances of perception, and psychomotor agitation. Recovery was obtained in 13 patients, and the 18 schizophrenic patients who completed the treatment were greatly improved. No complications were attributable to the treatment as carried out in the hospital by trained personnel. Convulsive seizures can be controlled by reduction of the dose. None of these patients developed paralysis agitans even when the daily dosage was 1.5 Gm. The authors concluded that promazine is a valuable drug in the treatment of mental diseases if the indications and contraindications are duly considered.

DENMARK

Antibiotic Resistant Staphylococci.—To determine whether the growing frequency of pencillin-resistant and streptomycin-resistant staphylococci was confined to hospitals, Eriksen and Dons (*Ugesk. laeger*, Oct. 8, 1959) examined 1,136 patients who attended the surgical polyclinic of the Rigshospital in Copenhagen to be treated for whitlows, abscesses, boils, and other subcutaneous staphylococcal infections between Oct. 1, 1949, and Dec. 31, 1958. Staphylococcus aureus was isolated in all the patients. In the period under review the penicillin-resistant staphylococcus rate rose from 10.0 to 57.6% and the streptomycin-resistant staphylococcus rate rose from 0 to 35.5%. Of the 1,136 patients, 814 had not previously been in contact with a hospital nor had they been given antibiotics, yet in this group the penicillin-resistant staphylococcus rate rose from 4.5 to 46.1%, and the streptomycin-resistant staphylococcus rate from 0 to 22.6%. These figures present a fairly accurate picture of what happens in the community as a whole with respect to antibiotic-resistant staphylococci.

Drug Poisoning.—In the past 25 years the changes in the treatment of drug poisoning have been so great that Dr. Carl Clemmesen (*Danish M. Bull.*, October, 1959) said that the methods of treatment used in the 1930's, if used now, would be regarded as malpractice, while omission of these methods at that time would have been similarly regarded. A decrease in the mortality from about 25% to between 1 and 2% has been achieved by the abandonment of methods enjoying a brief vogue. Early in the 1930's gastric lavage was done by some physicians using as much as 20 liters of water without obvious benefit. Artificial respiration in a respirator was so seldom successful that consignment to it came to be almost a death sentence. The vogue of stimulation with coramine lasted about 15 years, and the use of gastric lavage with charcoal lasted only about 5 years. It had driven the nursing staff half crazy because the charcoal-discolored fluid subsequently was spewed over bedclothes, walls, and nurses.

The concentration of all drug-poisoned patients in a single hospital in Copenhagen marked a new step forward. With the abandonment of stimulation, cases of cryptogenic hyperpyrexia ceased to occur, whereas such cases had previously often been fatal. In the past 25 years, the cases of poisoning coming to the hospital have reflected the prescribing habits of the medical profession, with the barbiturates being replaced in some instances by chlorpromazine and allied drugs. This is a change for the better, as the tranquilizers are much less dangerous than barbiturates.

"Dogger Bank" Itch.—In the last seven or eight years, Dr. A. Guldager (*Ugesk. laeger*, Oct. 8, 1959) examined 94 men and one woman suffering from "Dogger bank" itch, which has become a great nuisance among fishermen on the western coast of Denmark. It begins as red papules each about the size of a pinhead which appear on the volar aspect of the forearms up to sleeve level. Later it may spread to the face and neck and involve the eyelids and conjunctivas. It can be prevented by exploiting the observation that many acute allergic diseases of the skin such as urticaria and eczema respond well to the corticosteroids. Little can be expected of such prophylactic treatment while the disease is active, but after it has cleared up and the patient wishes to prevent a recurrence, the following procedure is effective: A 5-mg. tablet of prednisone is taken every eight hours when the fishing vessel leaves port. In the next two or three days, as the ship nears the fishing ground, the dosage is increased by one tablet daily. On the fishing ground 10 to 12 tablets are taken daily at the rate of one tablet every two or three hours. A break in this routine is so serious that an alarm should be sounded at regular intervals to ensure the patient's taking his tablets every third hour even throughout the night.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Staphylococcic Bacteremia.—At the Blegdam Hospital in Copenhagen, 51 patients with staphylococcic bacteremia were observed between 1940 and 1956 and 37 in the briefer period of 1957 and 1958. Dr. V. Faber (*Ugesk. laeger*, Oct. 15, 1959) noted that 41 of these 88 patients died. The lungs were involved in 59, the brain or meninges in 21, and the endocardium in 25. The infection was osteomyelytic in 21. In the last three years, isolated strains have been found to be penicillin-resistant in 75% of the patients, but only a few have been resistant to the tetracyclines. Faber advised the use of at least two antibiotics in high concentrations in treating such patients. Treatment should be continued for at least four weeks in view of the likelihood that the infecting organisms will develop resistance to the antibiotics given.

Peccant Staphylococcus Aureus.—Two articles in *Ugeskrift for laeger* for Oct. 15 by Dr. Ove Jessen and co-workers reflected the intensity of the campaign against pencillin-resistant staphylococci. The 222 strains isolated from patients with bacteremia were compared with those isolated from patients having impetigo and furunculosis and with strains from the noses of healthy carriers. Bacteremia was often traced to strains of bacteriophage groups 1 and 3, and while most of the strains were resistant to penicillin, resistance to the tetracyclines occurred mainly among strains of bacteriophage group 3.

The mortality from antibiotic-resistant strains was 50 to 60%. It was only 17 to 40% from antibiotic-sensitive strains. Bacteremia acquired in the hospital seemed to entail a graver prognosis than similar infections originating outside. In the period from 1938 to 1942, the bacteria most frequently isolated by blood culture at the State Serum Institute were nonhemolytic streptococci, Staphylococcus aureus, hemolytic streptococci, and Diplococcus pneumoniae. In the period 1953 to 1958, the most prevalent organisms were Staph. aureus, Escherichia coli, and nonhemolytic streptococci. Within the last six-year period an increasing proportion of the staphylococci isolated was antibiotic-resistant, but there was no marked change in the resistance of Esch. coli and nonhemolytic streptococci. In 1957 and 1958 there was a marked increase in the number of patients with bacteremia due to Esch. coli and Staph. aureus.

In the same issue Bang and Cowland reported a series of 457 members of a hospital staff whose noses were examined for staphylococci. Staph. aureus was found in 51.4%, and in 32.6% of these the staphylococci were found to be penicillin-resistant. Carriers of type 80 were treated with Topicin ointment (a mixture of 1% bacitracin and 0.5% neomycin) applied to the nasal vestibule morning, noon, and evening for two weeks. The number of type 80 carriers was reduced from 26 to 3.

Treatment of Lumbago and Sciatica.—Of a series of 182 patients with lumbago and sciatica only 32 were operated on. The remaining 150 were followed up by Frantzen and Zachariae (*Nord. med.*, Oct. 15, 1959), who noted that the conservative treatment given did not include extension or manipulation, emphasis being put on early mobilization and training of the muscles of the back. The traditional immobilization, prolonged after the cessation of pain, was discarded, and the patients rested on a hard surface. From one to four years after discharge, 17% were completely free from symptoms, 39% showed lasting improvement and another 39% showed temporary improvement. In several patients the irradiating pain had ceased while the back pain persisted unchanged. The authors did not say how those patients fared who were operated on, but they were sufficiently pleased with the results of conservative treatment to favor giving it a trial before resorting to operation.

Congenital Pyloric Stenosis.—Dr. J. Öster (*Nord. med.*, Oct. 15, 1959) reported that at the Randers Hospital 16 children admitted for congenital pyloric stenosis between 1949 and 1955 were treated conservatively with atropine methylnitrate. Thenceforth he changed to operative treatment with a view to achieving quicker results and assuring a better long-term prognosis, since others had shown that the children given only conservative treatment often developed dyspepsia and radiologically demonstrable signs of involvement of the pylorus, as well as motor disturbances of the stomach. All the 17 children admitted to hospital between 1956 and 1958 were operated on. The first of these had previously been given a course of conservative treatment. For the remaining 16 the duration of treatment in hospital was 30 days on the average as compared with the 49 days required by the earlier group. Of the 17 operated on 3 showed no roentgenographic signs of stenosis, yet it was demonstrable at the operation. Hence the suggestion is made that an x-ray examination, so trying for the child, may be superfluous in these patients.

GERMANY

Levallorphan Tartrate, a Morphine Antagonist.—G. Hohmann (*Ther. d. Gegenw.* 98:241-242, 1959) stated that investigations have shown that levallorphan tartrate inhibits or prevents certain characteristic effects of morphine. In small doses it counteracts the respiratory depression caused by morphine or morphine derivatives. This antagonism, however, does not extend to the respiratory depression caused by barbiturates or narcotic gases. In doses of sufficient size to relieve respiratory depression it does not have any noticeable influence on the analgesic effects. It probably acts by competitive inhibition in the sensory cortex and the respiratory center. The compound has only a slight analgesic effect and, in other respects, behaves differently from morphine. Thus in men and animals who have become habituated to morphine, it can cause typical withdrawal symptoms. Levallorphan is indicated for patients in whom it is desired to prevent or relieve respiratory depression, for example, in anesthesia or obstetrics (asphyxia neonatorum), for patients who are receiving large doses of analgesics for the relief of severe pain, in diagnostic or therapeutic operations on the bronchial tree, or for patients with overdosage or poisoning with morphine or its derivatives. Nausea and vomiting after treatment with morphine or its homologs can often be prevented by the compound.

Its duration of action is relatively short so that the depressive effect of morphine on the respiration may outlast the effect of the antagonist, necessitating repeated doses of the latter. Patients should, therefore, be watched carefully until normal respiration is reestablished. Hohmann used morphine or its derivatives postoperatively in combination with levallorphan to prevent respiratory depression. The patients were given a combined injection containing 4 or 5 mg. of a morphine derivative and 0.5 mg. of levallorphan before they left the operating room. The analgesic effect lasted in all patients at least five hours, and in no case was respiratory depression observed. This meant that the raising of sputum was facilitated and postoperative respiratory complications were greatly reduced.

The Use of Drugs in Urology.—H. Klosterhalfen (*Ztschr. Urol.*, vol. 52, no. 4, 1959) stated that in urology such neuroplegic drugs as chlorpromazine, promethazine, and thiazinamium are customarily used only for diseases originating in such disturbances of autonomic function as reflex postoperative or posttraumatic anuria. The antiemetic effect of chlorpromazine, which is mediated via the brainstem, has proved useful in the treatment of vomiting in patients with uremia and in overcoming otherwise intractable hiccupping. Since the tone and function of the bladder are chiefly under the control of the parasympathetic system, in patients with contracted or hyperirritable bladder (provided this is not due to irreversible organic changes) frequency of micturition can be relieved by the strongly parasympathomimetic drug, thiazinamium. The recommended dosage is from 0.6 to 1.2 Gm. a day, according to the initial level of the autonomic tone.

Inhibition of motor impulses can be so great as a result of treatment that paralysis of the detrusor muscle may be produced, with partial or total urinary retention. The strongly sympathomimetic drug, chlorpromazine, is said to be indicated in the treatment of simple ulceration of the bladder, since this condition is pathogenetically determined by trophic disturbances of the sympathetic system resulting in vasoconstriction. In order to include all segments of the autonomic reflex arc in treatment, it was recommended that chlorpromazine and thiazinamium be used in combination. In the treatment of inoperable carcinoma, especially carcinoma of the bladder, the phenothiazones proved of great value in view of their potentiating analgesic effect.

Brucellosis.—K. Bach (*Medizinische*, no. 23, p. 1109, 1959) said that before World War II the brucellosis produced by Brucella melitensis was unknown in Germany but that since then several cases have been reported in human beings, especially in southwestern Germany. The author reported an endemic involving six patients. The common source of infection was an aborting cow, which had been infected from the reservoir of infection in a large flock of sheep on the same farm. All the patients had more or less definite relapses even though they had been given adequate doses of antibiotics and steroid hormones. These relapses responded promptly to further antibiotic treatment. Late recurrences or a transition to the chronic form of the disease had not occurred when these patients were last seen.

Pemphigus Vulgaris.—E. Schlotter (*Hautarzt* **10**:173, 1959) used ACTH, cortisone, or prednisone in the treatment of a series of 20 patients who had pemphigus vulgaris. The levels of the initial, total, and maintenance doses were related to the severity of the disease and the site of the lesion. In order to produce a remission the following dosages were used: from 500 mcg. to 2.65 mg. of ACTH, from 900 mg. to 16.65 Gm. of Cortisone, and from 575 mg. to 2 Gm. of prednisone. The maintenance dose for prednisone was 7.5 mg. or more per day. One patient was given 150 mg. per day. Prednisone proved to be the most valuable. It was the least likely to produce side-effects and was the cheapest. More than 73% of the patients were still alive on a follow-up survey, which confirmed the fact that corticosteroid therapy improves the prognosis in patients with pemphigus vulgaris.

SWEDEN

Television Epilepsy.—The fact that epileptics are likely to respond to flickering light by an attack was known to slave dealers of old, the prospective purchase in the slave market being tested for epilepsy in this way. At the electroencephalographic laboratory of the psychiatric clinic of Malmö, Lagergren and Hansson (*Svenska läk.-sällsk. förhandl.*, Oct. 2, 1959) investigated suspected cases of epilepsy by photostimulation. Electroencephalograms enabled them to measure the degrees of photostimulation required for an epileptic response and to assess the part played by television in this respect. They reported three cases of epileptiform response to television in schoolgirls aged, respectively, 13, 12, and 14 years. To cut television entirely out of the lives of youngsters subject to television epilepsy would inflict a real hardship on them and amount to a psychic trauma, which the authors would avoid by laying down rules to be followed by susceptible persons. One rule is that of not staring at a well-lighted screen when sitting in a darkened room. Red eyeglasses help to filter off the long light waves that constitute the most epileptic-provocative part of the spectrum.

Kanamycin for Urinary Infections.—At two hospitals in Lund dealing with infections of the urinary tract, Dr. P. Erlanson and co-workers (*Svenska läk.-sällsk. förhandl.*, Oct. 16, 1959) gave kanamycin to 39 patients, 15 of whom suffered from chronic pyelonephritis, 14 from infections associated with operations on the urinary tract, and 10 from septicemia due to Staphylococcus aureus or coliform bacilli. The drug was usually given by deep intramuscular daily injections, the dosage being carefully adjusted to the degree of renal insufficiency in each patient. Serious impairment of hearing occurred in two patients with septicemia, and slight impairment in four of those with chronic pyelonephritis. The vestibular functions were also involved in the two with septicemia. The drug was most strikingly effective in obstinate cases of chronic pyelonephritis refractory to other antibiotics. The risk that this drug might cause organisms to become resistant to it seemed to be small, but it had little or no bactericidal action on streptococci, pneumococci, Pseudomonas, and anaerobic organisms. The drug may have a cumulative effect if more than 2 Gm. are given daily or if renal function is much reduced. For these and other reasons its use should be confined to hospitals, in which control of the dosage can be close and effective.

Acute Appendicitis in Children.—In a survey of a series of 686 children treated for appendicitis Dr. E. Sandegård (*Nord. med.*, Oct. 8, 1959) noted that none of these patients were less than one year old and that only 12 were less than 2 years old. All were operated on, the diagnosis being confirmed by macroscopic examination of the excised appendix. There were no deaths, although perforation with peritonitis was diagnosed in 140. In 6% of those with peritonitis and in 8% of those without perforation, other ailments, such as infections of the respiratory tract, were present. In 75% the leukocyte count was over 10,000 per cubic millimeter. The presence or absence of perforation had little effect on this count. Appendectomy was performed on 677 patients as soon as appendicitis was diagnosed. The remaining nine patients (all of whom had an appendiceal abscess) were operated on later when they were afebrile. The author concluded that with acute nonperforated appendicitis associated with high fever, it may be well to defer operation an hour or two to reduce the temperature to less than 38.5 C (101.3 F) by means of antibiotics and other measures. Peritonitis requires the most effective preoperative treatment, including relief of pain by a variety of devices. Such treatment often requires 4 to 8 hours, and on rare occasions 24 hours or more may be needed.

Gastric Polypi and Alopecia Areata.—Having found gastric polypi associated with alopecia areata in three patients, Dr. P. O. Andrell (*Svenska läk.-sällsk. fördhandl.* Oct. 9, 1959) wondered if he would find records of a similar association among the 18 patients operated on for gastric polypi at the St. Göran Hospital between 1951 and 1958. Four had died and another 4 could not be traced, but among the remaining 10 former patients alopecia areata was found in 3. This comparatively rare disease was observed in only 0.3% of all the patients being treated by the skin department of the hospital in 1951 and only 0.5% of those attending in 1952. The author believed that knowledge of this association may be helpful, with the diagnosis of alopecia areata serving as a clue in the diagnosis of polypi of the stomach.

Torsion of the Testis.—A series of eight patients, whose ages ranged from 2 to 19 years, was treated for torsion of the testis by Fahlström and Johansson (*Nord. med.*, Oct. 8, 1959). In three patients the torsion corrected itself spontaneously or under the influence of manipulation preparatory to operation. All three continued to be symptom-free. In another patient, aged 13 years, the torsion was corrected without an operation, but two or three days later renewed signs of torsion appeared. These again yielded to nonoperative treatment. On the recurrence of torsion a week later it yielded for the third time to nonoperative treatment, but to prevent further relapses the testis was secured in place by the Winkelmann operation. In three patients the testis was found on operation to be gangrenous. The most common erroneous diagnosis seems to be epididymitis, and the differential diagnosis is difficult enough to justify an exploratory operation in doubtful cases. The correct diagnosis may require an exploration which need cause no complications of an already existing epididymitis. Considering how quickly strangulation of a twisted testis may inflict irreversible changes on it, early operation is indicated when torsion is suspected.

UNITED KINGDOM

Hydroflumethiazide.—An annotation in the *British Medical Journal*, Nov. 7, commented on a paper in the same issue by Jones and Jones of Queen Elizabeth Hospital, Birmingham, on the diuretic effect of hydroflumethiazide. Until the advent of chlorothiazide, parenterally administered mercurial diuretics were unquestionably the treatment of choice for edema due to congestive cardiac failure. Millions of injections of mersalyl were given with a minimum of side-effects or toxic reactions. After intravenous administration sudden death due to ventricular fibrillation occurred in a score of patients, but unresponsiveness, sometimes associated with uremia, was not uncommon, especially when too stringent restriction of sodium intake was coupled with too frequent injections. But for the inconvenience of parenteral administration and the advisability of concurrent treatment with ammonium chloride to prevent hypochloremic alkalosis and unresponsiveness, mersalyl might still be the diuretic of choice. Acetazolamide, though not destined itself for a star position, pointed the way to a new series of potent diuretic agents that are effective when taken by mouth. Being predominantly a carbonic-anhydrase inhibitor, acetazolamide has a self-limiting diuretic action which ceases when excessive loss of bicarbonate (and potassium) in the urine induces a metabolic acidosis, and it can no longer be recommended for the treatment of edema.

Chlorothiazide was the first orally used diuretic to have a potency comparable with that of mersalyl, 2 Gm. by mouth being equivalent to about 2 ml. by intramuscular injection. Its ease of administration, flexibility of dosage, and ready acceptance by the patient have brought an understandable and worthwhile advance in diuretic therapy. The only important undesirable side-effect has been a tendency to hypopotassemia due to increased urinary excretion of potassium. This loss of potassium has been attributed to the mild inhibitory action of chlorothiazide on carbonic-anhydrase, but this cannot be the whole explanation, because excretion of bicarbonate does not parallel loss of potassium, which is severe only when sodium retention by the kidneys is marked. Furthermore, derivatives of chlorothiazide, which appear to have even less inhibitory effect on carbonic-anhydrase than the parent compound, also increase excretion of potassium. The chief importance of loss of potassium lies in the tendency of patients with hypopotassemia to develop digitalis intoxication. This is less likely to occur now that the practice, in early clinical trials, of giving too much chlorothiazide too frequently has been abandoned in favor of intermittent treatment, combined, if the patient is eating poorly or the edema takes more than 10 to 14 days to clear, with supplements of potassium on days when the diuretic is not given.

A number of derivatives of chlorothiazide have been introduced recently, and doubtless there are others yet to come. Making a choice may prove bewildering. The first derivative to be introduced was hydrochlorothiazide, and this was followed by hydroflumethiazide (hydrofluorochlorothiazide). These compounds, on a weight-for-weight basis, are more potent than chlorothiazide, but this is of no great advantage unless there is some superiority over the parent compound in the pattern of diuresis produced. Both hydrochlorothiazide and hydroflumethiazide have little or no inhibitory effect on carbonic-anhydrase, and so it was hoped that there would be no increased excretion of potassium in the urine. This has not proved to be the case with hydrochlorothiazide or hydroflumethiazide, which induced a fall in the serum potassium level below normal in 16 of 20 patients treated. Both of these derivatives should be given intermittently and supplements of potassium should be provided in the same circumstances as are necessary with chlorothiazide.

Chlorothiazide, or one of its derivatives, is the diuretic of choice in almost all patients with edema, both for initial therapy and, because of flexibility in dosage, for maintenance treatment. No one particular compound has any outstanding therapeutic advantage over another, and the practitioner is likely to use that with which he personally is most familiar.

Doctors' Hobbies.—The third annual Doctors' Hobbies Exhibition was marked by a higher standard than was the first exhibition in 1957, but with no less diversity. There were the inevitable stamp collections, photographs, homemade wines, model airplanes, and water colors, but the numerous oddities made the exhibition memorable: a sheepskin hat made from home-cured skins, a folding fishing-line dryer, a portable television set of midget size, and a steam-powered plant for a model cable ship. Probably the most macabre exhibit was the shrunken head of a Jivaro Indian. Other entries were two silver Regency nipple-shields, a coffee pot cozy, a tango in D minor, a single-deck motorcoach artfully converted into a luxury trailer for family holidays, a catamaran yacht, a Tibetan prayer-wheel, ships in bottles, knights in armor, a swarm box for bees with the entrance labeled "Bees this way please," and an exhibit on Esperanto.

First prize went to Dr. R. C. Bell for his book "Board and Table Games," which is to be published by the Oxford University Press. The second prize went to Dr. C. E. D. H. Goodhart for a collection of 17th century samplers, and the third went to Mr. R. C. Murray for a painting entitled "Return to Consciousness," which depicted the patient's eyeview. The technique for making a 1902 Caruso record sound like an up-to-date recording was a popular attraction for the many who possess a device which does the same thing in reverse.

Registration of Allied Professions.—The government's proposals for the statutory registration, professional education, and conduct of those practicing in eight professions allied to medicine were published in the profession's supplementary to medicine bill. It provides for a council and separate boards to be appointed. Each will have a disciplinary committee with power to strike practitioners off its register for crimes or professional misconduct. Those to be so regulated are chiropodists, dieticians, medical laboratory technicians, occupational therapists, physiotherapists, x-ray technicians, remedial gymnasts, and speech therapists.

CORRESPONDENCE

POLIOMYELITIS

To the Editor.—In a preliminary report on the surveillance of poliomyelitis from 1955 to 1959, Dr. Alex Langmuir and his colleagues indicated that since 1958 a new epidemiologic pattern of poliomyelitis has been emerging in the United States. They suggest that a basic change in the ecology of poliovirus may have occurred. The main features of this new pattern are described as follows:

> 1) Epidemics and outbreaks have been confined largely to specific focal areas composed of crowded population groups of lower socio-economic status [in which use of vaccine is likely to have been low]. 2) The age incidence has reverted, at least partially, to the infantile type. 3) Paralytic cases have occurred largely in unimmunized or incompletely immunized persons.

We have previously suggested that, despite the fact that Salk-vaccinated persons can become infected with poliovirus, adequate immunization with Salk vaccine might affect virus spread in the community. We would like to suggest now that the altered epidemiologic pattern of paralytic poliomyelitis in the United States may be the direct result of Salk vaccination's reducing the spread of virus. It is clear that Salk vaccination will not prevent alimentary infection with polioviruses, but what evidence have we that it does not cause a sufficient reduction in the virus excreted pharyngeally and fecally to lower the chances of spread?

To determine whether there is a significant average reduction in virus excretion at the critical time, a few days after infection, when dissemination is likely to occur is extremely difficult. An average reduction of fecally excreted virus, for example, from a titer of $10^6 TCD_{50}$ per gram to one of $10^5 TCD_{50}$ per gram may be sufficient to prevent transmission. To the best of our knowledge, whether this degree of reduction occurs has yet to be conclusively demonstrated. Could it be that recent outbreaks in the United States have been "confined to specific focal areas" as a result of Salk vaccination, which has prevented extension from these foci?

Since the type 2 antigen has, over-all, been the most effective component of Salk vaccine, it is reasonable to assume that Salk vaccination would have had most effect in limiting the spread of type 2 virus. Could the failure of type 2 virus to spread explain the fact that "the age incidence has reverted at least partially to the infantile type"? The reason for suggesting this is that recent infections with type 2 virus may give some measure of protection against a paralytic infection with type 1 virus. The reduction of type 2 virus in the community could mean that the unvaccinated "population groups of lower economic status" are not obtaining a natural immunity against type 2 virus and are thus subject to a greater probability of paralysis when they meet type 1 as their first poliovirus.

The present localized epidemics in the United States are somewhat reminiscent of "island type" outbreaks, in which a virulent virus is introduced into a susceptible community.

If one could be reasonably sure that the explanation for the altered epidemic pattern is as we have suggested, then it would seem reasonable that vaccination against poliomyelitis must be considered not simply as self protection but also as a public health measure for community protection. It could also be argued that there are dangers in the use of Salk vaccines with higher potency for type 2 than for type 1.

In 1955 Dr. Langmuir predicted that "If an effective vaccine becomes available and is widely used, then the proportion of susceptibles can be promptly lowered below the level that permits epidemic spread. Endemic spread alone will be insufficient to maintain survival. The infection must disappear." In 1957 he felt that these predictions were too optimistic, but he had anticipated an almost universal acceptance of the control procedure. We think that he may also have been influenced in 1957 by the knowledge that Salk vaccination did not prevent infection and excretion of virus. Was his 1955 prediction in fact correct?

Surely now is the time to put the hypothesis to the test. Will Salk vaccination "not only give a high level of protection to vaccinated individuals, but, if nearly every child is vaccinated, also to the community"? We think that "nearly every child" is essential, because poliovirus can spread through thinly populated districts, and that children are more important than adults, in this respect, because they appear to disseminate virus more readily.

If the hypothesis is incorrect, nothing but good can come of reducing the incidence of paralytic poliomyelitis in those vaccinated. If it is correct, then it will be of even greater benefit. Should a policy of perhaps free and universal vaccination be based on what is in fact no more than speculation? In this case we think it might be justified. What is there to lose?

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CLUSTER HEADACHES

To the Editor:—The editorial in THE JOURNAL, Oct. 31, 1959, page 1224, was an excellent review of an important topic. I feel, however, that my paper, "Ergotamine Tartrate Orally in Horton's 'Histaminic Cephalgia' (Also Called Harris's 'Ciliary Neuralgia'): A New Method of Treatment," published in Acta psychiatrica et neurologica scandinavica, supp. 46, 1947, pp. 105-113, has been overlooked. In this paper I gave the first description of what was later called the cluster pattern and also reported the introduction of prophylactic treatment with ergotamine tartrate during the periods of headache. In the ensuing years my findings were "rediscovered" several times by different authors mentioned in the editorial. The following lines from the summary of my paper corroborate what I have written above.

> Objections can be made to the name "histaminic cephalgia" and Harris's name "ciliary neuralgia" has never been generally accepted. The author has therefore called the condition Harris-Horton disease. In 13 cases (of 18) the disease ran a distinctly periodic course, the attacks of headache occurring for a few weeks or months at a time and then disappearing for many months or even years. This periodicity, which has hitherto been overlooked, must be considered when therapeutic results are evaluated. The author used a new form of treatment, viz. ergotamine tartrate orally. Sixteen cases were treated. As a rule two tablets of one milligram were given per day, occasionally three tablets. An immediate and considerable improvement was noted in 13 cases. Two cases showed no response, and 1 case was only slightly improved.

Anyone interested in this puzzling disease should read Robinson's outstanding review (Histaminic Cephalgia, *Medicine* 37:161 [May] 1958).

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ALLERGIC REACTIONS

To the Editor:—In the paper, "'Constitutional' Allergic Reactions and Their Prevention," in THE JOURNAL, Oct. 31, page 1172, the author lists intradermal skin testing as one of the major causes of constitutional reactions. My experience in testing many children, in the last 20 years, in the Allergy Clinic of the Children's Hospital of Michigan and in private practice, is that constitutional reactions are extremely rare if preliminary screening tests are done by the scratch method.

The author states, "It is fallacious to assume that preliminary scratch tests are a safeguard against constitutional reactions, which occur in spite of negative results of scratch tests, especially if the testing material employed by the scratch tests has lost its potency because it has been on hand too long." Experienced allergists do not make preliminary scratch tests with deteriorated materials. One must take exception to another statement in the paper, that infants and young children are more susceptible to constitutional reactions than adults. This is not in accord with the opinion of pediatric allergists. If the reaction to a properly performed scratch test is negative, an intradermal test can be performed safely, in a patient of any age, with the strongest material which will not give a nonspecific false-positive reaction.

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THE LONG GRIND OF MEDICAL EDUCATION

To the Editor:—In *Life* magazine, Nov. 2, 1959, page 95, in the article, "Why Medical Care Costs So Much," the following statement appears.

> Some administrators feel that the present long grind of medical education, especially the two to seven years a man spends as an interne and resident on coolie wages after medical school, actually encourages doctors to be cynical and mercenary. One hospital administrator said recently, "I have young doctors come into my office all the time who say, 'Well, I've worked my tail off here for four years for nothing—now I'm going out and get mine.' What we do is take an idealistic but inexperienced young person and in 10 years make him an experienced doctor but a bitter businessman." Even if the young physician entertains any notion about serving humanity and forgetting to send out his bills, he is likely to run into strong opposition from his wife. Having supported him through a good part of his medical education, reared the first baby or two in a dismal flat and gone without a car or a decent wardrobe for years, she can be pardoned for wanting a Cadillac and a fur coat. It might be better all around if young doctors were permitted to earn a living wage somewhat sooner.

This letter may serve to stimulate thinking and action in this remediable situation. The quoted extract from the article seems strikingly apropos.

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N. Y.

NO M.D.

To the Editor:—Perhaps, for the record, it would be wise for you to publish a correction to the Dec. 5 issue. In my letter on "Drug Names" I was given an M.D. degree. I do not have a doctorate in medicine.

CHAUNCEY D. LEAKE
Ohio State University
Columbus, Ohio.

Your original letter included no degree. I am sure that the manuscript editor was sufficiently aware of your interest in medicine over the years that she thought it would be proper to so honor you. I might well have had the same inclination, if this had been my responsibility.—ED.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Acute Idiopathic Pericarditis. M. M. Singer. Am. Heart J. 58:568-575 (Oct.) 1959 [St. Louis].

Singer points out that Barnes and Burchell in 1942 had called attention to the clinical similarity of idiopathic pericarditis and acute myocardial infarction and to the value of the electrocardiogram in the differential diagnosis. Singer reemphasizes this problem of differentiation by analyzing 15 cases of idiopathic pericarditis and presenting a detailed history of one patient, a 53-year-old man, who was hospitalized complaining of severe pain in the lower chest on the left, aggravated by deep inspiration. He had had a few similar attacks, beginning some 25 years before, and he had been told that he had "pleurisy." Interval chest roentgenograms revealed diffuse clouding over the left lower lobe, which was interpreted as a pleural reaction.

On the patient's admission in June, 1957, physical examination revealed decreased breath sounds and dulness to percussion over both posterior pulmonary bases. He was treated with penicillin, and the pleural effusions cleared. After that the heart was noted to be enlarged, but the patient was asymptomatic and was discharged. About 18 months later he was readmitted because of a sudden squeezing retrosternal pain which radiated to the left arm. Minimal rales were heard at the left posterior pulmonary base. Heart sounds were of diminished intensity, and no rub was audible. The electrocardiogram was interpreted as suggestive of anterior wall myocardial infarction, and the patient was treated accordingly. Basilar rales were interpreted as evidence of congestive heart failure. The patient slowly improved.

The 15 patients (13 men and 2 women) were observed between 1951 and 1958. Conventional 12-lead electrocardiograms and chest x-rays were taken. All the patients had pain, a pericardial friction rub, and/or a characteristic electrocardiographic pattern, but no specific demonstrable cause of pericarditis was seen. The chest pain was made worse by deep breathing in 8 patients and by change of body position in 6. S-T segment alterations characteristic of pericarditis were present in the electrocardiograms of 13 of the 15 patients. They had at least a 1-mm. S-T segment depression in lead aVR, usually early in the course of their illness during the phase of S-T elevation in the bipolar leads and before actual T-wave inversion in the precordial leads. This point is stressed because of its value in diagnosing acute idiopathic pericarditis when no Q waves are seen.

Modern Concepts Concerning Etiology and Treatment of Cerebrovascular Accidents. R. A. Kuhn. Angiology 10:342-354 (Oct.) 1959 [Baltimore].

The clinical syndrome known as stroke is a symptom complex representing cerebral dysfunction, which depends on various variables in the cervical-cerebral circulatory system. The author reports on 6 patients, with clinical and final diagnoses; the correct final diagnosis was made on the basis of serial cervical-cerebral angiography. Case 1. Clinical diagnosis: transient bouts of right-sided cerebral ischemia, etiology unknown; final diagnosis: a stenotic, almost nonfunctional right common carotid artery, most probably secondary to segmental arterial occlusive disease at its junction with the subclavian artery. Case 2. Clinical diagnosis: ischemic "stroke" with probable infarct of the right cerebral hemisphere; final diagnosis: space-occupying lesion in the right temporal lobe, most likely neoplastic. On operation, a malignant glioma of the right temporal lobe was excised. Case 3. Clinical diagnosis: repeated hemorrhages from aneurysm in the right anterior section of the circle of Willis; final diagnosis: aneurysm, right posterior communicating artery. Case 4. Clinical diagnosis: partial atherosclerotic occlusion of the right internal carotid artery at its bifurcation, with resultant slight left-sided "strokes" due to transient right-sided cerebral ischemia; final diagnosis: partial occlusion of the right internal carotid artery and complete occlusion of the right anterior cerebral arteries. Case 5. Clinical diagnosis: right-sided cerebral ischemia, probably affecting the thalamic area on the right, etiology unknown; final diagnosis: segmental arterial disease of the right vertebral and right internal carotid arteries, with occlusion of the central right vertebral artery. Case 6. Clinical diag-

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The place of publication of the periodical appears in brackets preceding each abstract.

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nosis: ischemia of the right cerebral hemisphere, etiology unknown; cerebral artery occlusion is probable; final diagnosis: segmental arteriosclerotic occlusive disease; severe right carotid cervical bifurcation. In most of these patients clinical means alone could have never established the correct diagnosis without the aid of serial cervical-cerebral angiography. Once the correct diagnosis was made, however, with this aid, beneficial therapeutic measures were instituted in all the patients.

Multiple Serial Enzyme Studies in Acute Myocardial Infarction. N. R. Rowell and A. J. Smith. Brit. M. J. 2:459-463 (Sept. 19) 1959 [London].

Serial daily estimations of the values bf serum glutamic pyruvic transaminase (SGP-T), serum aldolase, and serum oxidase for at least 10 days have been made in a series of cases of acute myocardial infarction. The results have been compared with similar estimations of serum glutamic oxalacetic transaminase (SGO-T) activity and with the erythrocyte sedimentation rate, temperature, and electrocardiogram. Estimations of these enzymes have been made in 50 healthy adults. The upper limit of normal (mean plus twice the standard deviation) in the present series was as follows: SGO-T, 28 units; SGP-T, 21 units; serum aldolase, 9.2 units; and serum oxidase, 372 units. Elevation of the SGP-T value occurred in 82% of the cases of myocardial infarction with a raised SGO-T activity. The rise occurred a day later, lasted a day longer, and was of much smaller degree than the rise in SGO-T value. Serum aldolase rose rapidly in almost all the cases of acute myocardial infarction; it reached a peak in 2 or 3 days and fell rapidly; a secondary rise occurred about 5 days after the initial peak. Serum oxidase rose gradually over the first 9 days, then remained steady for a few days, and fell to normal in most cases by the end of 3 weeks. There was no direct correlation with SGO-T levels, and serum oxidase remained normal while SGO-T levels were markedly elevated. No consistent correlation between the erythrocyte sedimentation rate, temperature, or electrocardiogram and the secondary rise in serum aldolase or the rise in serum oxidase was observed. Coronary insufficiency without infarction did not alter the level of SGO-T or SGP-T. Elevations of the levels of SGO-T, SGP-T, serum aldolase, and serum oxidase may occur in cardiac failure with centrilobular necrosis of the liver.

A Study of Combined Mitral and Aortic Stenosis. J. F. Uricchio, K. P. Sinha, L. Bentivoglio and H. Goldberg. Ann. Int. Med. 51:668-678 (Oct.) 1959 [Lancaster, Pa.].

The authors present a review of the clinical and hemodynamic pattern in 141 patients treated by combined mitral and aortic commissurotomy between 1953 and 1958. There were 52 men and 89 women, ranging in age from 23 to 67 years, who had mitral and aortic stenosis, either alone or in combination with adynamic, physiologically insignificant aortic and mitral regurgitation. The analyses of the complete symptomatic patterns, including the electrocardiograms and chest roentgenograms, were compared with those obtained from 2,000 patients with pure mitral stenosis and from 350 patients with pure aortic stenosis.

Associated dyspnea and fatigue were present in nearly 9 out of 10 patients with combined mitral and aortic stenosis, as well as in the patients with isolated mitral or aortic stenosis. Six or 7 patients out of 10 with pure mitral stenosis had edema. Three out of 10 patients in the combined group presented hemoptysis; 2 out of 10, emboli; and nearly 4 out of 10, nocturnal dyspnea. Syncope was twice as common among patients with isolated aortic stenosis as among those with combined lesions. Typical coronary pain occurred in almost half of the patients with aortic stenosis, and in only 23% of those with combined mitral and aortic stenosis. A rough murmur of aortic stenosis was heard in all the patients, but in only 22% of them was the second sound, as heard over the aortic area, normal, because the fibrotic and calcific process had not completely eliminated valvular mobility. The ancillary signs of mitral stenosis were often unimpressive, but the murmur was heard in almost every patient.

The heart size was significantly increased in more than 8 out of 10 patients. The electrocardiogram revealed a pattern of right, left, or combined hypertrophy in 4 out of 10 patients. Cardiac catheterization demonstrated similar valve areas in the combined and isolated obstructive valve lesions. Cardiac output was compromised to a greater degree in patients with mitral and aortic stenosis. Marked elevation of the calculated pulmonary resistance and mean pulmonary artery pressure was not encountered among the patients with mitral and aortic stenosis. Lower systolic ejection gradients were found in patients with combined disease than in those with pure aortic stenosis.

Physiologic and Biochemical Aspects of the Disordered Coronary Circulation. R. Gorlin, N. Brachfeld, J. V. Messer and J. D. Turner. Ann. Int. Med. 51:698-706 (Oct.) 1959 [Lancaster, Pa.].

The authors studied the hemodynamic and biochemical characteristics of the coronary circulation in 50 patients; 10 of these patients were judged to have nearly normal hearts, 23 had angina pectoris, and the remaining 17 had varying states which imposed an increased work load on the left or the right ventricle. Electrocardiograms were recorded, following exercise, in all patients with clinical chest pain, both at the time of catheterization and as part of a standard exercise two-step test. Coronary flow was shown to depend upon the need for oxygen by the heart, and this, in turn, to be related to the hemodynamic and metabolic factors of that moment. Glyceryl trinitrate (nitroglycerin), while causing a coronary vasodilatation in patients with normal hearts, failed to do so to any extent in patients with angina pectoris. Exercise had a variable effect in patients with angina pectoris. In those with no clinical pain or electrocardiographic changes, the increase of coronary flow was adequate to the needs. In patients with angina and depressed S-T segments, myocardial ischemia was evidenced by a fall in coronary venous oxygen saturation and the appearance of both lactate and pyruvate in coronary venous blood. Effects of glyceryl trinitrate in patients with angina pectoris are probably attributable to modification of cardiac venous return and contractility, and depression of hemodynamic change on effort.

Addison's Microcardia. N. De Pasquale, G. La Rosa and N. Puglisi. Minerva med. 50:2494-2499 (Aug. 11) 1959 (In Italian) [Turin, Italy].

A study of patients with Addison's disease, who were observed for a long period of time before and after treatment with hormones, is reported. Microcardia was the most typical and constant clinical sign observed during the active phase of the disease; a markedly increased lung-heart ratio was a constant roentgenologic sign. Microcardia was also found to be an important sign in evaluating the effect that treatment with hormones was having on the patients. Marked changes in the diameters and in the volume of the heart were observed while the patients were being treated with hormones. A careful control of these changes helped avoid the risk of unexpected consequences that may result from an excessive dose of hormones; usually accidents, such as cardiac failure, are preceded by an increase in the volume of the heart. The suspension of hormonal treatment for a long period of time and the return of the symptoms of Addison's disease were usually accompanied by a return of microcardia.

Atherosclerosis Obliterans of the Extremities and Coronary Insufficiency: Clinical Study of 134 Cases. A. Buzzi. Prensa méd. argent. 46:915-918 (April 10) 1959 (In Spanish) [Buenos Aires].

The incidence of alterations in the coronary circulation associated with atherosclerosis of the extremities was studied in 134 patients—131 men and 3 women, between the ages of 37 and 80 years. The diagnosis was established clinically on the presence of intermittent claudication, cold extremities, continuous or paroxysmal pain at rest, retrosternal or precordial oppressive pain, and absent or diminished peripheral pulse. Each patient underwent electrocardiographic examination, including the 6 leads of the extremities. The magnitude and intensity of the symptomatology were analyzed, as well as the reciprocal influence between angina pectoris and intermittent claudication.

Electrocardiographic alterations were found in 73 patients. In 20 of these there were signs of myocardial infarction, while in 34 the alterations involved the S-T segment and the T wave but not any pathological Q wave. This last group was considered, from the electrocardiographic point of view, as having chronic coronary insufficiency, although the possibility of an anatomic myocardial necrosis was not excluded. The majority of the 34 patients with these electrocardiographic alterations suffered from angina pectoris alternating with intermittent claudication. In some patients the anginal attack was accompanied by a false sensation of relief from the claudication, which resulted from the imposed rest and restricted physical activity. In others the claudication was a late symptom and masked the coronary insufficiency. In 19 patients there were electrocardiographic signs which indirectly suggested alterations of the coronary circulation. In this group there was complete auriculoventricular block in 1 patient, right bundle-branch block in 8, and left bundle-branch block in 10. The probability of a coronary etiology in these patients was supported by the presence of angina pectoris in 50% of them.

Only a limited number of patients were followed up; in some the disease took an unusual malignant course, ending in early sudden death. The total incidence of demonstrable electrocardiographic alterations in this series of patients was 54.4%. The author concludes that patients who suffer from thromboembolic complications usually succumb in consequence of a coronary, rather than a peripheral vascular, accident.

An Appraisal of the Latex Test for Rheumatoid Arthritis. M. R. Jeffrey. J. Lab. & Clin. Med. 54:525-534 (Oct.) 1959 [St. Louis].

Outpatients of the department of medicine at Tulane University, for whom a diagnosis of rheumatoid arthritis, arthritis, or related diseases had been established, were given latex agglutination tests. Normal serums were obtained from students and staff of the medical school. Control serums were taken from patients attending the hematology or cancer detection clinics, who were free from any arthritic manifestations. Three degrees of agglutination were recognized: fine (x), which could be seen with certainty only through hand lens; moderate (xx), which was clearly visible to the naked eye; and coarse (xxx), which showed obvious clumps and clear background. The 76 patients with rheumatoid arthritis (19 men and 57 women) had a much higher proportion of positive tests than any other group, and showed a sex difference. All the men had a positive test at a dilution of

1:20 of both serum and euglobulin. Of the 57 women, agglutination occurred at 1:20 in 45 (79%) serum and in 53 (93%) euglobulin specimens. The differences were not likely to be fortuitous either at 1:20 or 1:160 dilutions of serum or at 1:160 dilution of euglobulin. The patient's age and the duration of the disease were not important. Of 9 patients (4 men and 5 women) who were tested between 3 and 12 months after the onset of their disease, all the men and 2 women gave titers of 1:160 in serum and euglobulin; 2 other women gave lower titers. In 18 women who had arthritis of at least 10 years' duration, 10 showed agglutination at 1:160 in serum or euglobulin, 6 gave lower titers, and 2 were negative. The treatment did not apparently affect the agglutination results.

The other groups receiving the test were composed, respectively, of patients with juvenile rheumatoid arthritis, osteoarthritis, other types of arthritis, collagen diseases, and minor rheumatic disease. Comparison of the results showed that, except for 2 patients with systemic lupus erythematosus, marked agglutination (xxx) occurred only with the serum and euglobulin fractions of patients with rheumatoid arthritis. All the rheumatoid specimens lacked inhibitory activity at 1:14 dilution after inactivation. Of the specimens selected at random from the other disease groups, more than one-third lost inhibitor activity during inactivation. The latex agglutination test appears to be at least as accurate as the sheep-cell technique in the diagnosis of rheumatoid arthritis, and it has some technical advantages.

Alkaptonuria and Ochronosis. J. Červeňansky, Š. Siťaj and T. Urbánek. J. Bone & Joint Surg. 41-A:1169-1182 (Oct.) 1959 [Boston].

This report is based on observations made on a group of 22 families who exhibited hereditary alkaptonuria. The disease was present in 119 persons, and 36 of these (22 males and 14 females) had ochronotic arthropathy. Alkaptonuria is a hereditary disease, and every patient in whom this diagnosis was made led to the discovery of a new case. Since all of the affected families came from mountainous areas and from villages in which endemic goiter is prevalent, it may be of interest that tyrosine is the precursor not only of homogentisic acid but also of thyroxin. Alkaptonuria may be manifested only by the excretion of homogentisic acid, which may go on for decades before other symptoms supervene. The latter are due to the deposition of the homogentisic acid derivatives in many tissues, which then turn black or brown, hence the term "ochronosis." It is assumed that the ochronotic pigment is caused by oxidation and polymerization of homogentisic acid, probably by way of the enzyme tyrosinase.

There was a rising incidence of ochronosis among patients of the 3d, 4th, and 5th decades, after which the incidence decreased. The earliest manifestation was ocular and auricular pigmentation, but the most important clinical symptoms of alkaptonuric ochronosis were those in the joints. These usually first appeared in the spine when the patients were between the ages of 30 and 40 years. There was an indefinite sensation of stiffness in the lumbosacral region accompanied by some tenderness. In 6 patients the initial complaints were acute radicular pain similar to sciatica. In general, the arthropathy began insidiously without marked symptoms. The spine showed a gradual flattening of the physiological curves. Later, there appeared a fixed, rather sharp kyphosis in the lower thoracic or upper lumbar region, often involving only 2 or 3 vertebrae; this was accompanied by decreased mobility of the spine. This degree of involvement was reached in about 3 to 5 years after the first joint symptoms were experienced. With further evolution a striking kyphosis was seen. Eventually, both the lumbar and the thoracic spine became rigid and ankylosed. The patients were considerably shorter than the average person in the local population.

The knee joints became involved in 64%, the shoulder joints in 42.3%, and the hips in 34.6% of the patients with ochronotic arthropathy. Ocular ochronosis did not include visual disturbances. Homogeneous brownish blue spots were found in the scleras, and granules of pigment were seen in the bulbar conjunctivas and along the temporal and nasal margin of the corneas. Pigmentation of the corneas was a pathognomonic finding in ochronosis. In the ear, not only were pigment collections found in the auricle, but lesions involving the tympanic membrane, external auditory canal, and middle and inner ear were also seen. In the trachea and bronchi, ochronosis at times manifested itself only by discoloration of the cartilage rings, without any symptoms.

Since alkaptonuria is thought of as a metabolic disorder involving proteins, dietetic methods have been stressed. Starvation leads to a decrease of the amount of homogentisic acid in the urine, although it does not completely prevent alkaptonuria. Overloading with dietary protein increases the homogentisic acid in the urine. The results of therapeutic trials of restrictions of protein require long-term evaluation of many patients. Because of the influence of vitamin C on the metabolism of tyrosine and phenylalanine, a group of 15 patients with arthropathy were given ascorbic acid daily and a standard diet of 2,200 calories with 80 Gm. of protein. The excretion of homogentisic acid was not influenced even by the highest doses of ascorbic acid. While the treatment with ascorbic acid did not prevent the increased alkaptonuria caused by the administration of 5 Gm. of tyrosine daily, and whereas the intensity of the pigmentation was not influenced, the symptoms of the arthropathy were favorably affected. Although the alkaptonuria persisted, the urine was not dark because it was kept acid, the ascorbic acid inhibiting the oxidative changes.

The following drugs were administered to patients without significant effect: folic acid, vitamin B_{12}, liver extract, raw liver, cystine, and methionine. The administration of 4-methyl-2-thiouracil resulted in a decrease of alkaptonuria and in a remission of clinical symptoms in 2 patients; sudden withdrawal of the drug led to an acute relapse in 1 patient; maintenance doses achieved lasting benefit in 1 of 2 other patients. Symptomatic measures consisted of massage, heat, and analgesic drugs. Arthroplasty was employed when indicated for severe joint deformity.

Remission in Diabetes. A. Bloom. Brit. M. J. 2:731-734 (Oct. 17) 1959 [London].

The author reports on 344 women and 206 men with newly diagnosed diabetes mellitus, who were referred to the diabetic unit at Whittington Hospital, London, between 1952 and 1957. Of the 550 patients, 287 (52%) were between the ages of 40 and 65 years, 82 (15%) were younger than 40 years, and 181 (33%) were older than 65 at the onset of the disease. One hundred eighty-four (33.4%) of the 550 patients were adequately controlled by dietary restriction from the start; these were overweight patients with mild diabetes, who were instructed concerning a 1,200 or a 1,500 calorie diet according to the degree of obesity, and were also instructed as outpatients to test the urine for sugar. As a rule, the diet was increased up to 2,000 calories when weight had been lost. One hundred forty-five patients (26.3%) were ultimately controlled by dietary restriction alone after temporary treatment with insulin or tolbutamide. The diet in this group varied from 1,500 calories (about 150 Gm. of carbohydrate, 65 Gm. of protein, and 70 Gm. of fat) to 2,200 calories (about 232 Gm. of carbohydrate, 82 Gm. of protein, and 105 Gm. of fat). The patients usually received 1 Gm. of tolbutamide twice a day initially, and the dose of the drug later was reduced to 0.5 Gm. 3 times daily or twice a day. The remaining 221 patients (40.2%) needed permanent treatment with insulin or tolbutamide. Insulin was given to patients in whom there was infection or gangrene, to those who failed to respond to tolbutamide, and to those with severe diabetes whose urine contained acetone.

With few exceptions, young underweight patients with diabetes mellitus need continuous insulin therapy. Older patients with mild diabetes and overweight respond to simple carbohydrate dietary restriction without adjuvant therapy. Between these 2 groups there are many patients with diabetes whose cases are neither so severe as to need immediate or permanent treatment with insulin nor so mild as to be satisfactorily controlled by dietary restriction alone. Since its introduction, tolbutamide has been extensively used in the treatment of mild diabetes mellitus, and so far no serious toxic effects have been reported.

The dangers of unnecessary prolongation of insulin therapy are exemplified by 2 cases of "post-hypoglycemic encephalopathy" in a 63-year-old woman and a 75-year-old man. The woman had self-administered a mixture of 24 units of soluble and 24 units of zinc protamine insulin each morning for years. On admission to hospital, she was confused and incontinent, and had spastic extremities and extensor plantar reflexes. This condition continued for 12 days, even though the blood sugar level became normal; control of her diabetes was subsequently obtained with 20 to 30 units of insulin zinc suspension daily, and the dose of the drug was later reduced to 10 units, on which the urine remained largely sugar-free and the blood sugar concentration was normal or near normal. The man who had mild diabetes had self-administered 22 units of zinc protamine insulin daily for years. He was admitted to hospital because of mental confusion and incontinence, which persisted for nearly 2 weeks despite withdrawal of insulin. He left the hospital in full possession of his mental faculties and did not require insulin. Hypoglycemic encephalopathy appears to have been induced by unnecessary administration of insulin.

Kartagener's Syndrome with Fibrocystic Disease. N. M. Brown and A. N. Smith. Brit. M. J. 2:725-728 (Oct. 17) 1959 [London].

The authors report on a 20-year-old man who was admitted to the Western Infirmary in Glasgow for a persistent severe pain in the left iliac fossa, associated with anorexia, nausea, and a temperature of 99.4 F (37.4 C). Tenderness in the left iliac fossa was accompanied with hyperesthesia. The patient had marked finger clubbing. There was dulness and moist rales at the right base; the apex was palpated in the 5th right interspace, 3½ in. (9 cm.) from the midsternal line, and liver dulness was present on the left. A diagnosis of acute appendicitis with transposition of the viscera was made, and appendectomy was carried out through a left iliac fossa incision. Abnormal rotation, the absence of the pelvic colon, and the presence of the liver on the left side of the abdomen were confirmed. A roentgenogram of the chest showed dextrocardia and a left-sided aorta; the left dome of the diaphragm was higher than the right, probably owing to a left-sided liver. Bronchograms showed a bronchiectasis of the left lower lobe and lingula. The frontal sinus was underdeveloped, and there was thickening of the mucosa in both maxillary antrums.

Analysis of the electrolyte composition of sweat from the patient showed abnormally high values for sodium chloride within the accepted range for fibrocystic disease of the pancreas recorded by di Sant' Agnese. The ratio of split to unsplit fat in the patient's stool and its nitrogen content showed deviation from normal values.

The history of this patient with situs inversus revealed that he had had repeated attacks of pulmonary infection related to bronchiectasis and sinusitis, the syndrome described by Kartagener in 1933. The patient was thought to have mucoviscoidosis or fibrocystic disease of the pancreas, since he had bronchiectasis, sinus infection, and anomalies of the sweat excretion and the exocrine secretion of the pancreas, consistent with this diagnosis. One of the siblings of the patient also showed abnormal losses of sodium chloride in the sweat. Since many patients with mucoviscoidosis can have the latent type of disease and may pass unrecognized in the community except by the sweat-composition defect, it is possible that association between situs inversus and mucoviscoidosis is more common than one believes. It might be that the Kartagener syndrome is a form of situs inversus associated with fibrocystic disease, and, if searched for, concomitant defects, such as faulty exocrine secretion of the pancreas and sweat, will be found in patients with the congenital defect of situs inversus. It is supportive evidence for this concept that the defect in sweat composition was found in another member of the patient's family.

Hydatid Disease. C. L. Birch and B. P. Anast. J. Am. M. Women's A. 14:885-896 (Oct.) 1959 [New York].

Hydatid disease is caused by the larval forms of 2 types of small tapeworms, Echinococcus granulosus and Echinococcus multilocularis. Man is an accidental intermediate host. In the domestic cycle of E. granulosus, the usual intermediate hosts are sheep, hogs, and cattle, and the definitive host is most commonly the dog. Man acquires the infection by ingesting the ova of E. granulosus, which hatch in the duodenum, liberating the oncospheres which penetrate the wall of the intestine. Most of the larvae are filtered out in the liver, but some pass on to the lungs and other organs. Many are destroyed by tissue reaction and phagocytosis. Most of those that are screened out in the liver survive as spherical or irregular vesicles or cysts.

A single hydatid cyst may become very large and is usually filled with clear fluid. The wall is lined by a parasitic germinative membrane that buds off scolices. Some of the buds are lined by germinating epithelium that buds off scolices of its own, forming brood capsules that break from the lining membrane and float in the cyst fluid, forming the so-called hydatid sand. Sudden rupture of the cyst, either spontaneous, surgical, or traumatic, may cause death, probably from the anaphylactic reaction to the antigenic cyst fluid. If death does not follow rupture immediately, the dissemination of fluid spreads the disease, since each scolex or grain of hydatid sand has the potential power to produce a hydatid cyst. In hydatid infection of the lung, hooklets may be found in the sputum. If the kidney is involved, they may appear in the urine. If a hydatid cyst of the liver ruptures into a bile duct, hooklets and portions of the cyst wall may be found in the stool.

Of the 6 patients with hydatid disease, whose histories are presented, the disease in 5 was caused by E. granulosus and in 1 by E. multilocularis. In 2 of the patients the diagnosis was made by roentgenography, and in 4 by surgical section and microscopic study. Three of the patients were immigrants (1 from Poland, 1 from Greece, and 1 from the Ukraine), and 3 were born in the United States and spent their lives here. It has been suggested that E. multilocularis is identical with E. sibiricensis. Two endemic areas on the North American continent have been identified, one in northern Canada and Alaska and one in the lower Mississippi Valley, including the states of Mississippi, Tennessee, Louisiana, and other southern states. In one year, April, 1957, to April, 1958, a packing company in Jackson, Miss., slaughtered 33,153 swine; of these, 305 (or 0.92%) were infected with E. granulosus. In southern and central Mississippi the percentage of infected animals was as high as 4.03%. Experiments showed that dogs could be infected, and that they passed gravid proglottids and ova as early as 46 days after inoculation. No dog showed any symptoms, even when harboring 1,000 worms.

SURGERY

Operative Versus Nonoperative Treatment of Massive Hemorrhage from Peptic Ulcer. W. A. Johns and H. P. Royster. Am. Surgeon 25:730-732 (Oct.) 1959 [Baltimore].

The authors report on 2 groups of patients with hemorrhage from peptic ulcer, in whom a remarkable similarity with regard to age, location of ulcer, and hemoglobin levels on admission to hospital was established. The first group consisted of 136 patients who were treated at the Medical College of Virginia Hospital in Richmond between 1947 and 1957; of these, 19 had gastric ulcer, 6 had stomal ulcer, and 111 had duodenal ulcer. The average age of these patients was 52 years; the youngest was 17 years old, and the oldest was 84. The average hemoglobin concentration on admission was 49% (7.4 Gm. per 100 cc.). Of these patients, 47% were Negroes. There were 17 deaths, and 11 of these occurred in Negroes. Selective gastrectomy was employed in the treatment of massive upper gastrointestinal hemorrhage, and 33 of the 136 patients were operated on during the acute phase of hemorrhage. Subtotal gastrectomy was performed on 31 patients, and gastrectomy and vagotomy on 1; a sleeve resection was performed on 1 elderly poor-risk patient. Seven of the 19 patients with gastric ulcer died; 4 of them were operated on, and 3 were not. Ten of the 111 patients with duodenal ulcer died; 5 of them were operated on, and 5 were not.

The second group consisted of 117 patients who were treated at the Johnston-Willis Hospital in Richmond during the same period; of these, 15 had gastric ulcer, 2 had stomal ulcer, and 100 had duodenal ulcer. The average age of these patients was 52 years; the youngest was 18 years old, and the oldest was 89. The average hemoglobin concentration on admission was 50% (7.5 Gm. per 100 cc.). There were 4 deaths in this group. Conservative therapy, consisting of bed rest, administration of antispasmodics and antacids, frequent feedings, and administration of opiates and sedatives, was started on admission and was continued; *surgical treatment* was *not employed during the* acute phase of bleeding.

Despite inherent discrepancies between these 2 groups of patients, some of which were not amenable to quantitative analysis, more favorable results with nonoperative therapy during the acute phase of the hemorrhage seem apparent. Since operation was generally selected for severe or persistent hemorrhage, the fact that in the group in whom selective gastrectomy was employed 8 deaths occurred in patients not operated on suggests that the need exists for emergency gastrectomy in some cases. The findings point to the need for more critical selection of these cases and to the difficulty in reaching an early decision as to whether surgical treatment will be necessary in a given patient. More prolonged medical management seems to be indicated, with surgical intervention being reserved for those patients in whom it is necessary as a lifesaving procedure, or in whom it seems obvious that conservative treatment will be unsuccessful. Elderly patients, especially those with gastric ulcer, are less likely to respond to conservative therapy and should be considered more strongly for immediate gastrectomy. Death due to exsanguination in patients aged less than 50 years is extremely rare with proper medical treatment. The deaths which occurred, in both surgical and nonsurgical patients, have been associated with coronary occlusion, renal ischemia, hepatic failure, aspiration pneumonia, atelectasis, pneumonitis, cardiac arrhythmia, and congestive failure. Gastrectomy after cessation of hemorrhage and restoration of blood volume is a comparatively safe procedure and should be employed in the prevention of recurrent hemorrhage.

True Operative Mortality in Simple Suture of Perforated Gastroduodenal Ulcer. A. Ciminata. Minerva chir. 14:1053-1054 (Sept. 15) 1959 (In Italian) [Turin, Italy].

The results obtained with simple suture in 135 patients operated on for perforated gastroduodenal ulcer in the surgery department of the Hospital of Monza, Italy, are reported. The author points out that his series included all the patients with perforated gastroduodenal ulcer observed in this department during a 10-year period from 1948 to 1957, irrespective of the type of perforation, of the extent of *peritoneal involvement,* and of the condition of the patients. Six male patients (4% of the whole series) died. The first patient, 57 years of age, was operated on 72 hours after perforation had occurred, and died of peritonitis on the 2nd postoperative day; the second, 48 years of age, was operated on 70 hours after perforation, and died of peritonitis on the 2nd postoperative day; the third, 60 years of age, was operated on 48 hours after perforation, and died of peritonitis on the 7th postoperative day; the fourth, 43 years of age, was operated on 24 hours after perforation, and died of pneumonia on the 6th postoperative day; the fifth, 59 years of age, was operated on 18 hours after perforation, and died of pneumonia on the 5th postoperative day; the sixth, 58 years of age, who was suffering from severe myocarditis, was operated on 12 hours after perforation, and died of ventricular fibrillation on the 6th postoperative day.

The first 3 patients, operated on from 48 to 72 hours after perforation, were considered by the author as being in a preagonal condition. The "true mortality rate," therefore, was zero among the patients operated on during the first few hours after perforation, and 2.5% among the patients operated on within 24 hours after perforation. The reasoning that *simple suture does not lead to complete recovery,* while *resection does, seems* unwarranted to the author, who believes that the patient with a perforated ulcer should be saved from imminent death by a nondangerous operation, such as simple suture, which may be performed by any surgeon.

Some Experiences with Stenosis of the Sphincter of Oddi. J. A. Kirtley Jr., L. A. Grossman and D. H. Riddell. South. M. J. 52:1167-1171 (Oct.) 1959 [Birmingham, Ala.].

The diagnosis and correct treatment of stenosis of the sphincter of Oddi or atresia of the papilla of Vater are still controversial. Narrowing of the ampulla or papilla of Vater may be the only pathological finding on exploration of the common duct and ampulla of Vater. Del Valle was probably the first to section the sphincter of Oddi to relieve this stricture-like obstruction. This report deals with 31 patients who had obstruction at the sphincter which prevented the passage of a 3-mm. Bakes dilator. There were some patients in whom the dilator was "tight" in the ampulla, but successively larger dilators, up to 5 or 6 mm., could be passed without undue pressure. These patients were not included, and their symptoms have been relieved by the dilatation alone.

The 31 patients included 16 who previously had had cholecystectomy, 8 who had "idiopathic stenosis" of the sphincter without stones in the gallbladder or the common duct, and 7 who had cholelithiasis or choledocholithiasis associated with stenosis. All these patients were subjected to transduodenal sphincterotomy, with good results in 25 of the 31. It would seem that stenosis of the sphincter or atresia of the papilla of Vater is a definite, and possibly the most common, cause of the "postcholecystectomy syndrome." This same stenosis or atresia may cause similar symptoms in patients having normal cholecystograms and was found to coexist in 7 patients who had stones in either the gallbladder and/or the common duct preoperatively. A definite diagnosis based on positive laboratory or radiographic findings may be difficult. Exploration of the common duct is indicated when the symptoms and/or operative findings are suggestive of stenosis. Transduodenal sphincterotomy has been a satisfactory procedure in relieving preoperative symptoms. Pancreatitis with fat embolism may be a serious complication. More experience is needed to determine which patients undergoing initial gallbladder surgery or patients with symptoms of gallbladder disease should have supraduodenal exploration of the ampulla and, if resistance to the smallest dilator is encountered, which surgical procedure is then indicated.

Observations on Bile Secretion in Human Subjects: Report of a New Method for Continuous Registration of Bile Secretion. G. Mollowitz. Arch. klin. Chir. 291:359-398 (no. 5) 1959 (In German) [Berlin].

Reviewing the methods available for studying the quantitative course of the bile flow, the author felt that they involve too many sources of error. He accordingly developed a new technique, which he first described in 1954-1955. His method employs a transcholedochal tube with a T-drain, blockage of the distal part of the choledochus with foam rubber, and continuous automatic registration of the bile flow with a device which incorporates a rain-gauge recording drum. He describes his experiences with this device in 100 patients who were operated on for calculi in the extrahepatic bile passages. Cholecystectomy was carried out in all the patients, or it had been performed at an earlier operation. The choledochus was opened in all the patients, and in 30 patients only T-drainage was used, but in the remaining 70 patients the T-drainage was combined with the transcholedochal tube. In 25 of the 70 patients blockage of the duct was added, and in 10 of these the bile flow was recorded continuously for the duration of the period of drainage. The effect on bile secretion of 3 different choleretics was investigated.

It was found that the liver produces bile uninterruptedly. Immediately after an operation on the bile passages the bile production is reduced, but usually it returns in the course of 8 or 9 days to a stable level. The diurnally excreted quantities of bile differ greatly from patient to patient, and there are also considerable fluctuations in individual patients. A profuse bile production that remains uniform throughout the period of observation involves no danger, provided that the bile is not lost to the organism. Liver failure threatens if a rapid increase in bile production is followed by a great decrease in the secretion.

Bile excretion is subject to rhythmical fluctuations during the 24-hour period, and this diurnal rhythm is impaired immediately after the operation. Disease of the liver may cause disturbances in the diurnal rhythm, and as a result the flow may be almost uniformly continuous day and night. The administration of fluids, either enterally or parenterally, has no influence on the bile flow. The intake of food normally increases bile secretion, but when the liver is diseased, it does not respond as effectively to the food stimulus. During fasting the diurnal rhythm persists, although in a somewhat reduced form. The choleretic effect of the 3 agents tested was very slight or could not be demonstrated; in the dosage given, they did not increase the bile flow of the patients operated on during the period of observation.

The author feels that his method gives a better insight into the bile secretion of patients operated on than was possible with earlier methods. Since he realized that external bile drainage is not physiological, this factor was counteracted by reinfusion of the bile. The negative results of the use of choleretics convinced him that after operations they cannot be expected to increase bile flow. The fact that the method gave early information about impending liver failure is expected to improve further the therapeutic results.

Development of Metastases after Removal of Primary Malignant Tumors. A. Prudente. Rev. brasil. cir. 38:153-159 (Aug.) 1959 (In Portuguese) [Rio de Janeiro].

The possibility of dissemination of neoplastic cells after a biopsy or an operation is an unresolved issue in cancerology. In relation to the biopsy problem, the author reports a comparative study of 2 groups of patients with carcinoma of the breast treated by radical mastectomy. Each group was composed of 30 patients. Those in the first group had had frozen section biopsy, and those in the second group had had a preliminary biopsy. In the frozen section biopsy group there were 16 survivors (53%) without recurrence, whereas in the preliminary biopsy group there were only 12 (40%). The latter group was then subdivided into 2 groups according to the interval between biopsy and mastectomy. Of 18 patients who had undergone operation within a few days to a month after the biopsy, 9 survived and were asymptomatic, while of 12 patients who had been operated on within 1 to 7 months after the biopsy, only 3 had survived without recurrence. The author interprets this difference as an indication that during the longer interval before the operation the disease had advanced to a much more serious stage.

In relation to metastases which seem to be induced by the removal of the primary tumor, the author reports a group of 14 patients who underwent amputation for osteogenic sarcoma. Eleven patients developed pulmonary metastases within 6 months after removal of the tumor. None of them had shown any metastases before the operation, although in some the primary tumor had been developing for 1 to 4 years. The development of postoperative metastases may be due to the existence of neoplastic cells which are "quiescent" while the primary tumor absorbs certain specific substances. With removal of the tumor, there is an abundance of specific nutrient substances available to the disseminated cells, thus inducing their development. The absence of metastases prior to the operation was a result of an athreptic immunity. The following elements are probably related to the development of postoperative metastases: (1) existence of neoplastic cells in circulation; (2) existence of small groups of cancerous cells in the capillaries of different organs; (3) existence of a specific defense mechanism in the cells and absence from the blood; and (4) existence of a certain number of circulating cells representing a threshold which varies with the type of tumor.

For prevention of postoperative metastases, the author recommends a combined treatment with chemotherapy and radiation, preoperatively and postoperatively. The preoperative treatment may destroy the disseminated, "quiescent" neoplastic cells and cause a regression of the tumor, which will make the operative condition more favorable. Favorable results were obtained with this type of treatment in an 11-year-old girl with osteogenic sarcoma and in a 32-year-old man with a kidney tumor.

Sarcoma of the Small Intestine. K. Kettunen. Ann. chir. et gynaec. Fenniae 48:390-399 (no. 3) 1959 (In English) [Helsinki].

The author reports 8 cases of sarcoma of the small intestine, a tumor of rare incidence. There were 2 children in this group, one 5-year-old boy and one 14-year-old boy. The other 6 patients were 2 men and 4 women, between the ages of 40 and 67 years. Clinical symptoms were scarce in all the patients. Hemorrhage, manifested either by blood in the stools or by secondary anemia, was present in 5 patients; intussusception, with varying degrees of obstruction with cramping colicky pain, in 3; and mild diarrhea, in 3. In one patient the only symptom referable to the gastrointestinal tract was meteorism. In 3 patients the tumor was palpable. Roentgenologic examination was the most decisive diagnostic procedure. The roentgenologic signs of small intestinal sarcoma can be summarized as destruction and obliteration of mucous membrane pattern, stiffness of the wall, and absence of peristalsis.

The prognosis was poor in all these 8 patients because of extensive mesenteric involvement. They underwent laparotomy, with removal of the tumor, and resection of the small intestine; there was end-to-end anastomosis in 3 patients, side-to-side anastomosis in 4, and ileotransversostomy in 1. In 6 patients the operation was followed by radiation therapy. The longest survival was obtained by a 54-year-old man who was asymptomatic for approximately 5½ years after removal of his reticulum-cell sarcoma. At the second operation a tumor was found originating in the jejunum, approximately 10 cm. from the previous enteroanastomosis. The patient died one month after completion of the radiation therapy which followed the operation. The shortest survival was that of the 5-year-old boy who died approximately 3½ months after the initial symptoms and operation.

Effect of Perphenazine on Postoperative Emesis. L. C. Cutolo and N. H. Kleppel. A. M. A. Arch. Surg. 79:666-669 (Oct.) 1959 [Chicago].

Emesis during the immediate postoperative period creates 3 major hazards: dehydration, electrolyte imbalance, and delayed alimentation. The authors report on 57 male and 51 female patients, between the ages of 14 and 74 years, who underwent surgical treatment of an average duration of 1½ hours. Of the 108 patients, 32 received perphenazine (Trilafon) preoperatively and 30 received perphenazine one hour postoperatively to protect them against postoperative emesis. Thirty-two patients received perphenazine therapeutically only if vomiting had occurred, and 14 patients did not receive perphenazine. A single dose of 5 mg. of the drug was administered intramuscularly. Nausea or vomiting occurred in 9 of the 14 untreated patients, an incidence of 64%; it occurred in 16 of the 32 patients who received the drug therapeutically, an incidence of 50%. The incidence of nausea or vomiting thus did not differ significantly between these 2 groups of patients. The incidence of nausea and vomiting in the group of 32 patients who received the drug preoperatively was 12%, as compared with 10% in the 30 patients who received perphenazine one hour postoperatively. The over-all incidence of nausea and vomiting in the group of 46 patients who did not receive prophylactic treatment was 54% (25 patients), in contrast to 11% in those who received prophylactic treatment (7 of 62 patients). When emesis did occur among treated patients, the total period of nausea and vomiting was shorter in duration, and the individual attacks were less severe and less frequent.

Patients who received perphenazine tolerated fluids by mouth earlier than did those in the contratest series. Perphenazine also proved to be effective in the treatment of the 32 patients with nausea or vomiting after operation. Emesis usually ceased within 30 minutes after administration of the drug. There appeared to be no hypotensive effect attributable to perphenazine. Patients who received perphenazine were genrally more relaxed and comfortable during recovery. In addition, postoperative administration seems to cause drowsiness, an effect which is usually desirable.

Perforation of Peptic Ulcer into Free Peritoneum: Clinical and Therapeutic Aspects in 66 Cases. H. A. Soares, O. B. Tourinho and J. Toledo. Rev. brasil. cir. 38:95-116 (Aug.) 1959 (In Portuguese) [Rio de Janeiro].

Sixty-six patients with perforated peptic ulcer underwent emergency operation at the hospital of the Institute of Previdencia Social in Rio de Janeiro during the period 1953-1958. There were 65 men and 1 woman in this series, with ages ranging from 20 to 61 years. The great majority (75.5%) were in the under-50 age group. In 14 patients (20%) there had been no symptoms or signs of ulceration until the perforation. Of the 52 patients with a clinical history of peptic ulcer, 32 had never received any medical treatment, but had used home medicines. In the untreated group the interval between the first symptoms and the perforation was much shorter than in the treated group. Including the 14 patients who had been asymptomatic, the untreated group represented 67.3% of the patients in this series.

Symptoms of an impending perforation were observed in 24 patients (36.3%), who during 1 or 2 weeks prior to the acute accident felt an aggravation of the pain, accompanied by flatulence, nausea, vomiting, intolerance to certain foods, with hematemesis and melena in a few patients. Symptoms of the perforation were acute pain and rigidity of the abdominal wall. Collateral symptoms were vomiting, abdominal distention, intestinal obstruction, hematemesis, and melena. Forty-nine (72.3%) of the perforated ulcers were gastric, and 17 (24.6%) were duodenal. Preoperative medication consisted of the administration of antibiotics, maintenance of the sodium balance, administration of vitamins A and C, blood and plasma transfusions, and administration of amino acids. In the great majority of the patients (81.5%) the surgical technique comprised simple suture of the ulcer with epiploplasty; the remaining patients underwent immediate subtotal gastrectomy. The operative mortality rate was 11% among the patients who underwent conservative surgery, and 8% among those who had undergone gastrectomy. A follow-up of 25 patients showed that 12 were clinically asymptomatic, and 10 were still suffering from peptic ulcer symptoms. Three patients were subjected to gastrectomy in a second operation within 2 to 6 months after the first. Three patients died of unknown causes within 6 to 12 months after the operation.

Myxoma of the Left Atrium Simulating Restenosis of the Mitral Valve. M. Deshmukh, H. Nichols and H. Goldberg. Am. Heart J. 58:623-629 (Oct.) 1959 [St. Louis].

The patient was a 47-year-old woman who was admitted to the Hahnemann Hospital, Philadelphia, in September, 1958, with complaints of easy fatigability, exertional dyspnea, intermittent palpitations, and swelling of the ankles, which responded to mercurial diuretics and digitalis therapy. About 4 years ago, in December, 1954, a diagnosis of rheumatic heart disease with mitral stenosis had been made, and the patient had been subjected to mitral commissurotomy. At that time a dilation of the left atrium had been noticed. After "finger fracture" of the mitral valve, the biopsy report stated that the left atrial appendage was normal atrial muscle. The postoperative course of the patient was uneventful except for the development of chest pain, which was considered to be part of the postcommissurotomy syndrome. Surgery was followed by a brief period of improvement, but then shortness of breath and fatigability resumed and progressed.

The clinical picture and the physiological studies were consistent with restenosis of the mitral valve, and the patient was regarded as a suitable candidate for mitral commissurotomy. The left atrium was approached through a thoracotomy incision on the right, and during exploration of the left atrium a huge tumor, occupying most of the left atrial cavity, was palpated by the exploring finger. Because of the extreme friability of the tumor, and because of fear of producing systemic emboli, the definitive procedure was postponed until a later date, and the chest was closed. Another operation was performed 12 days later. A pump-oxygenator to bypass the heart was preferred to the closed-heart technique or hypothermia. The tumor was removed completely, and the woman had an uneventful recovery.

The clinical picture, physical findings, and laboratory investigations in this case were entirely consistent with refusion of the mitral valve. None of the features that have been suggested in the literature as indicative of myxoma of the left atrium were present in this patient, but the authors suggest that a faint diastolic murmur in patients presenting a clinical picture of mitral stenosis should make one suspicious of the possibility of the presence of a tumor in the left atrium. These tumors are extremely friable, and their removal under direct vision is necessary if systemic embolization is to be avoided during surgery. The use of a pump-oxygenator is of distinct advantage over hypothermia in an adult or elderly patient, and this should be the method of choice in the removal of this tumor.

Pancreatic Endocrine Function and Peptic Ulceration. R. M. Zollinger and D. W. Elliott. Gastroenterology 37:401-411 (Oct.) 1959 [Baltimore].

The authors report on 75 patients with "ulcerogenic adenoma" of the pancreas, whose cases were collected from the literature and in whom a clinical triad, consisting of fulminating ulcer diathesis, massive gastric hypersecretion, and a nonbeta, noninsulin producing adenoma of pancreatic islet cells, was substantiated by clinical findings. Usually definitive methods of ulcer therapy—medical, irradiation, and surgical—are all doomed to failure while gastric mucosa remains under the influence of this ulcerogenic adenoma. Tests by which such an adenoma may be diagnosed preoperatively are not available. However, a strong suspicion of its presence should be entertained (1) whenever a peptic ulcer is found in an unusual location, particularly in the jejunum; (2) whenever massive gastric hypersecretion is shown on 12-hour aspiration; (3) whenever other endocrine hyperfunction is encountered in the ulcer patient; or (4) when an ulcer recurs promptly after adequate surgical intervention for ulcer. The pancreas should be carefully searched for adenoma in every patient undergoing operation for intractable peptic ulcer, particularly if the ulcer has recurred after usually acceptable therapy. If there is good reason to suspect that an ulcerogenic adenoma of the pancreas is present and none can be found, the body and tail of the pancreas should be resected for adequate histological study. Diffuse insular involvement or hyperplasia may be found.

If an ulcerogenic adenoma can be proved to be present, total gastrectomy is the operation of choice at this time. This is because of the great difficulty and uncertainty of removing all functioning adenomatous tissue. Microscopic occult functioning adenomas or metastases can doom any ulcer treatment short of total gastrectomy to failure. The authors report 2 clinical cases, one in a 44-year-old woman and the other in a 19-year-old woman, to illustrate this principle. In the older woman the diagnosis of an ulcerogenic tumor of the pancreas, for which this patient was admitted to the Ohio State University Hospital in Columbus, was suggested by the repeated perforation of jejunal ulcers. The extremely high volume of gastric secretions on 12-hour aspiration also supported this diagnosis. Excision of all visible pancreatic tumor and removal of both antral and cephalic stimuli for gastric secretion failed to control the gastric hypersecretion and ulcer diathesis. At a second operation the total pancreas was removed in the hope of ablating all functioning tumor, but the operative specimen showed tumor tissue even beneath the mucosa of the duodenum. Perhaps other functioning metastases accounted for the ulcer diathesis persisting till all gastric mucosa was removed; if so, these metastases were so small as to escape detection even at autopsy. Although the patient survived and maintained her weight for nearly one year with no stomach and no pancreas, fatty infiltration of the liver resulted, with debility that eventually resulted in death. One cannot escape the impression that, if total gastrectomy had been performed when the diagnosis of ulcerogenic tumor was first established, the older woman might have escaped the later total pancreatectomy and its consequences, labile diabetes and hepatic degeneration. Furthermore, total gastrectomy then would have been a far more certain means of aborting the ulcerogenic potential of the residual adenomatous tissue than the attempt to excise it. This principle is especially evident if one compares the course of this patient with that of the younger woman in whom perforating jejunal ulcers and truly massive gastric hypersecretion also were findings characteristic of an ulcerogenic adenoma of the pancreas. Removal of both antral and cephalic stimuli for gastric secretion failed to control a fulminating ulcer diathesis, while a gastric pouch, measuring only 6 by 8 cm., remained in the presence of a functioning adenoma. Total gastrectomy restored this patient to reasonable health, even though metastases of her islet-cell carcinoma were present at the time of this operation. In 3½ years since, no evidence of recurrence of this malignant adenoma has appeared.

Surgical Aspects of Occlusive Disease of the Aorta and Iliac Arteries. A. W. Humphries, V. G. deWolfe, F. A. Lefevre and R. C. Britton. Ann. Int. Med. 51:686-697 (Oct.) 1959 [Lancaster, Pa.].

The authors present experiences with 750 arterial grafts in the aortoiliac and femoral areas, which led them to follow certain criteria in selecting candidates for arterial surgery. Before deciding whether a patient should be subjected to an arterial reconstruction, it should be determined whether surgery is technically possible. Successful restoration of blood flow depends on a new blood supply from a proximal site and also on the distribution of this new supply to the distal vessels. If the patient's own terminal distributional system is not patent, the circulation will not improve. In the segmental type of occlusion, the continuing vessels are open, and the blood supplied by the graft has a means of egress. In the nonsegmental form, there is no distal point to which the graft may be attached, and surgery is not feasible. The length of the occlusion is not particularly important, but the presence of adequate outflow is critical.

Intermittent claudication, the mildest of the symptoms of arterial insufficiency, may lead to progressive claudication, and should be treated surgically. Further involvement beyond the stage of simple claudication occurs if the arteriosclerotic occlusive process extends, or if a thrombosis in situ is superimposed on a sclerotic stenosis, in which case the symptom of rest pain or the development of an ulcer or even gangrene may supervene, and the need for restoration of the arterial flow is acute; however, in many instances the outflow tract may no longer be open, and a graft cannot be done. Patients not suitable for direct arterial surgery may be divided into 2 subgroups: those with associated prohibiting disease, such as congestive heart failure, malignancy, and incapacitation due to previous stroke, and those with arterial involvement too minimal to require correction. Patients with angina must be carefully evaluated, and a decision made between the benefits to be derived from a satisfactory graft and the possible aggravation of cardiac insufficiency from the stress of the operation. Patients with angina decubitus should never be subjected to grafting.

In this study of 750 arterial grafts followed up to 5½ years, all the grafts for aneurysms have remained open, 90% of the elective aortoiliac grafts for occlusive disease still function, 80% of the nonelective aortoiliac grafts are patent, and almost 70% of the femoropopliteal grafts remain successful. Most of the failures in this series occurred within the first year after placement of the graft. Advancement of the patient's own disease below the lower limits of the graft has been the most common cause of failure.

Use of Autogenous Lung in Extracorporeal Circulation: Experimental Study and Clinical Application. G. Blanco, E. Rey-Baltar and others. Rev. clin. españ. 74:93-96 (July 31) 1959 (In Spanish) [Madrid].

The authors have developed a modification of the autogenous lung tissue technique as the source of blood in heart surgery under extracorporeal circulation. Instead of using the cardiac lobe, as did Cohen and Lillehey, they use the right upper lobe. The venous blood is sent from the venae cavae directly into the pulmonary artery. The arterial blood is drained (through only one catheter inserted into the left auricle) either by pump suction or by flowing freely into a reservoir at a lower level. From this reservoir the blood is again perfused into the arterial system.

This technique, developed in experimental studies on dogs, was applied in the treatment of 20 patients with either aortic stenosis or aortic insufficiency. The operation consisted in separating the valve commissures and removing the plaques of calcium from the semilunar valves. In 4 patients with aortic insufficiency the posterior Valsalva sinus was removed with its semilunar valve, and the aortic valve was converted into a functional bicuspid valve. The first 8 patients were operated on under induced heart arrest. The results were favorable in the first 5 operations, but failure of recovering the heart contractions in 3 patients led to abandoning the heart-arrest technique and to using a direct continuous perfusion of the coronary arteries with arterial blood.

As a consequence, the arterial blood is taken from the extracorporeal circle which goes into the femoral artery and sent through a pump into the coronary system. The volume of coronary perfusion is 200 to 250 cc. per minute. An artificial oxygenator is at hand for emergencies, such as functional failure of the autogenous lung. A second pump is used for suction of a certain amount of blood which enters the left ventricle as the heart keeps contracting rhythmically during the operation. Eight of the 12 patients operated on according to this modified technique recovered. The authors consider these results as encouraging; they recommend further investigation for continued improvement of the technique.

The Management of Abnormal Bleeding Following Extracorporeal Circulation. H. A. Perkins, J. J Osborn and F. Gerbode. Ann. Int. Med. 51:658-667 (Oct.) 1959 [Lancaster, Pa.].

The authors studied the effects of various techniques of extracorporeal circulation on the blood coagulation system of 125 patients who were operated on with the aid of heart-lung bypass machines. Reports by other workers on the hematological effects of heart-lung bypass were collected from the literature. Although the improvement in heart-lung bypass machines has made abnormal postoperative bleeding unusual, a hemorrhagic state may still occur in a variety of circumstances. Severe thrombocytopenia may be induced by the use of improperly cleaned equipment, or by the administration of excessive amounts of bank blood with nonviable platelets. Inadequate neutralization of heparin or, in rare cases, administration of excessive amounts of protamine may result in a hemorrhagic state. Fibrinolysis was not observed by the authors in their patients, but remains a possibility. Bypasses of more than 2 hours in duration and traumatic bypasses may result in depletion of some coagulation factors, with involvement particularly of the first stage of coagulation. It is important to remember that this coagulation defect is spontaneously reversible. No therapy is required, therefore, except to replace the blood as it is lost through the chest drainage tube, preferably with fresh blood in plastic bags or siliconed bottles.

To avoid abnormal bleeding and to manage it if it nonetheless occurs, the following coagulation studies are recommended. Before the operation is performed with the aid of extracorporeal circulation, the history of the patient for bleeding tendency should be checked. If the history is at all suggestive, any laboratory tests necessary to rule out a coagulation defect should be performed. A blood sample should be drawn at the time of the first visit to determine the patient's blood type for cross-matching. Observation of the time it takes this blood to clot will provide additional information as to the possible presence of a coagulation defect. If there is no evidence to suggest a hemorrhagic diathesis, checking of blood platelets on the blood smear obtained at the time of hospital admission is enough to rule out thrombocytopenia of any consequence. If bleeding is present after the operation, a protamine titration and a platelet count should be done. The patient should undergo reexploration, with the expectation of finding one or more bleeding points that need ligation, if the results of the titration test indicate a normal clotting time, proper heparin neutralization, and a good firm clot, if there is an adequate platelet count, and if, despite this, bleeding persists to a grossly unusual degree.

Surgical Management of Gastric Cancer: Results in a 10-Year Period (1948-1957). P. Nogueira, L. A. Sant'Anna and E. R. da Silva. Rev. paulista med. 55:21-35 (July) 1959 (In Portuguese) [São Paulo, Brazil].

The authors treated surgically, during 1948-1957, 82 patients with gastric cancer. Forty-four operations were a subtotal gastrectomy, and 12 were a total gastrectomy; 4 patients had gastroenterostomies, and 22 were subjected to simple exploratory celiotomies with lymph node biopsy. There were 64 men and 18 women, with ages ranging from 20 to 80 years; the great majority belonged in the 40-60 age group. No early diagnosis had been established for any patient. The most striking and common symptom had been pain, especially thoracic or lumbar. Less frequent were anorexia, postprandial disturbances, nausea ,and vomiting. In some patients the insidious onset and asymptomatic course were present until the advanced degree of the lesion which allowed only a palliative treatment. Dysphagia meant an unfavorable prognosis associated with a late diagnosis. Cytological examination of the gastric contents obtained by lavage failed to establish the diagnosis. Roentgenologic examination was performed on all the patients and was unrevealing in only 3.

The surgical approach was mainly abdominal, which the authors consider to be less traumatic and requiring less time. In subtotal gastrectomy the conservation of a small cardiac area of 2 to 3 cm. prevented enteroesophageal reflux. This technique was used when the lesion was situated in the distal half of the stomach. In total gastrectomy the continuity of the intestinal tract was accomplished by the interpolation of a jejunal loop. In the total gastrectomy group (12 patients), there were 2 postoperative deaths caused by dehiscence of the esophagojejunal anastomosis. At the time this article was written there were 11 survivors from the subtotal gastrectomy group (44 patients) and 3 from the total gastrectomy group. These figures represented, in the first group, a survival of 6 to 8 years in 3 patients, of 5 years in 3, and of 4 years in 5. In the second group there were 2 survivals of 3 years and 1 of 8 years. Among the patients who were dead at the time of the follow-up, 33 who had undergone subtotal gastrectomy had survived from 1 to 3 years; among the 7 who had undergone total gastrectomy, 1 had survived 4 years, 3 had survived 2 years, and 1 had survived 1 year.

Recurrent Carcinoma of the Stomach Seventeen Years After Subtotal Gastrectomy. C. D. Cobau, R. J. Bartlett and H. M. Pollard. Gastroenterology 37:427-433 (Oct.) 1959 [Baltimore].

The authors report on a 79-year-old man who was admitted to the University Hospital in Ann Arbor, Mich., in July, 1958, for supportive and terminal nursing care necessary because of rapid, recent debilitation due to proved generalized metastatic disease. The patient had been operated on at the same hospital in June, 1941, at the age of 62, for a poorly differentiated adenocarcinoma, grade 3, which was prepyloric and on the posterior surface of the stomach. There were several enlarged mesenteric nodes as well as lymph nodes along the common duct and the posterior surface of the stomach, and in the gastrohepatic ligament. The entire lower half of the stomach, the pylorus, and 1 in. of the duodenum were removed. During the next several years the patient was evaluated at frequent intervals, either during outpatient visits or by the neoplasm follow-up unit. At no time was there evidence of recurrence or metastases from the original carcinoma. About 17 years after the gastric resection, a few months before his readmission to the hospital, the patient had noted the appearance of a mass in the epigastric area, with associated anorexia, fatigue, and generalized malaise. One week before readmission, a marked and steady epigastric pain had progressed to the point of being unbearable. A biopsy of the mass revealed well-differentiated adenocarcinoma forming many gland-like spaces.

Despite supportive therapy, the patient's course in the hospital was progressively downhill, and he died. At autopsy the portion of the stomach remaining after the two-thirds gastric resection showed marked atrophy of the mucosa with apparent hypertrophy and dilatation of the lumen. At the line of the anastomosis between the small intestine and the residual stomach, there was a mass conforming to the lines of resection and measuring no greater than 2 cm. in width. The neoplasm appeared to be mucosal and not an extrinsic mass invading this portion of the stomach from the serosal aspect. It was largely confined to the gastric side of the anastomosis. The abdominal, retroperitoneal, and mediastinal lymph nodes were extensively involved, and the liver was about 80% replaced by a metastatic neoplasm. Microscopically, the gastric neoplasm was a moderately well-differentiated adenocarcinoma. The sections of the operative specimen of 1941 were reviewed and compared with the autopsy findings, including the gastric adenocarcinoma. The latter was considered a "much more differentiated neoplasm," but the possibility that this was a long-term recurrence could not be excluded on this basis.

Eleven similar cases in which the patients survived 12 years or longer were collected from the literature. Lack of nodal involvement at the time of the subtotal gastrectomy, dissimilar histological appearance, and an exceptionally long period of latency have been cited to support the view that the second carcinoma was unrelated to the original lesion. The authors' patient had 2 of these features, namely, different histological findings and long latency. Although the findings in this patient do not permit a definite conclusion as to the origin of the second carcinoma, the authors believe that this represents a long-term recurrence. This opinion is based on evidence of involvement of lymph nodes at the time of the original resection. The patient's course serves to illustrate the great variability in the natural history of this disease.

The Management of Radiation Injuries to the Intestines. J. I. Fabrikant, W. G. Anlyan and R. N. Creadick. South. M. J. 52:1186-1191 (Oct.) 1959 [Birmingham, Ala.].

The authors present observations on 71 patients with "factitial proctitis," who were observed at Duke University Hospital, Durham, N. C., from 1933 to 1955 inclusive. During this period more than 2,700 patients with carcinoma of the cervix were treated with either radium, roentgen rays, or a combination of the two. Fifty-nine patients subsequently presented intestinal symptoms, a complication rate of 2.1%. The remaining 12 patients had been treated for abdominal or pelvic malignancies. In 7 instances the signs and symptoms of radiation enteritis and proctitis appeared immediately, and in 24 cases such stigmas were manifest within 6 months of the conclusion of radiation therapy. The longest interval prior to onset of symptoms was 20 years, and in 3 patients more than 10 years had elapsed. The mean interval was 13 months.

The most frequent intestinal symptoms were pain on defecation, diarrhea, and the passage of blood and mucus. The symptoms did not progress in 50 of the patients, and conservative therapy proved adequate. Late complications included the formation of fistulas (rectovaginal, vesicovaginal, ileosigmoid, and ileovaginal), hemorrhage, and stenosis, with partial or complete intestinal obstruction. Patients treated initially with roentgen irradiation had the highest incidence of fistula formation. Permanent colostomies were done in 18 patients, 13 of whom had rectovaginal or vesicovaginal fistulas, or both. Eight of these patients experienced immediate and progressive improvement, but 3 did not, and 7 others died of metastatic extension of their disease. A portion of the terminal ileum was resected in 4 patients, and of the jejunum in 1, because of obstruction, and the symptoms were relieved immediately.

The treatment of choice for irreversible radiation enteritis is resection of the damaged segment with primary anastomosis. Permanent colostomy may be required if the complications of rectovaginal and vesicovaginal fistulas, hemorrhage, or obstruction become progressively worse and threaten the life of the patient. The management of factitial radiation proctitis and enteritis requires close cooperation between surgeon, gynecologist, and radiotherapist.

Functional Restoration in Synovial Tuberculosis of the Knee: Treatment and Results. W. Legal and R Pfeiffer. München. med. Wchnschr. 101:1675-1678 (Sept. 25) 1959 (In German) [Munich, Germany].

When tuberculosis of the knee joint is restricted to the synovial membrane, the therapeutic measures are quite different from those that are necessary when the bony structures are likewise involved. Whereas, with bony involvement, surgical fixation is usually resorted to in patients in whom the tuberculous process is restricted to the soft capsular tissues, treatment should aim at restoration of the normal motility. Among 114 patients with tuberculosis of the knee joint, hospitalized in a department of extrapulmonary tuberculosis between 1947 and 1958, there were 67 with involvement of bone and cartilage, whereas in the remaining 47 the tuberculous process was limited to the soft tissue of the capsule. In many instances the diagnosis could be based on the clinical and roentgenologic aspects. When it was doubtful, it was verified by exploratory excision and histological studies or by bacteriological examination of the punctate. The authors resorted to exploratory excision of the capsule of the knee joint for diagnostic purposes in 94 patients, in 33 of whom it resulted in the diagnosis of tuberculosis, either restricted to the synovial or involving the osseous tissues.

In evaluating the results of the treatment of synovial tuberculosis of the knee, the authors eliminated 14 of the 47 cases in which the treatment remained incomplete. The treatment described combines orthopedic measures with chemotherapy. First, the joint is immobilized in a plaster cast, until the signs of acute inflammation have subsided and the blood sedimentation rate has returned to normal. In early cases immobilization for about 3 months is usually adequate. During and after immobilization, intensive combination chemotherapy is continued for 4 months. For the first 6 weeks adults are given isoniazid daily by mouth in doses of 10 mg. per kilogram of body weight, and in addition 1 Gm. of streptomycin by intramuscular injection. For the remaining 2½ months only oral therapy is given, in the form of Nicoteben (a combination of isonicotinic acid hydrazide [Neoteben] and isonicotinic aldehyde thiosemicarbazon) in daily doses of 5 mg. per kilogram of body weight. The authors do not advise intra-articular injections, because the repeated injections are not without danger, and patients generally dislike them. The immobilization in a plaster cast is followed by intermittent extension therapy, during which the weight is removed daily for gradually increasing periods, and active movements without weight bearing are attempted. After 3 more months, extension is discontinued, and several weeks later exercise with weight bearing is begun.

The described treatment was employed in 17 of the 33 patients with synovial tuberculous gonitis. In 9 of these patients the results were excellent, and in 3 others good; in 4 the improvement was "still adequate"; the result was unsatisfactory in only one patient, a 60-year-old man. The results achieved in this group are very favorable in comparison with the results of the preantibiotic conservative therapy or of synovectomy.

A New Concept in The Treatment of Malignant Melanoma. R. F. Ryan, E. T. Krementz and O. Creech. Plast. & Reconstruct. Surg. 24:349-356 (Oct.) 1959 [Baltimore].

With wide local excision and regional node dissection, the salvage rate among patients with malignant melanoma has gradually improved, but local recurrence and wide dissemination unfortunately are still common. Irradiation and endocrinotherapy have been ineffective. Systemic chemotherapy has produced dramatic temporary regression of malignant melanoma in some instances, but no cures have resulted. In 1957 the authors began experiments to develop techniques for isolating and perfusing tumor-bearing areas with cancericidal drugs. The techniques offer the following advantages: 1. The drug can be administered intra-arterially. 2. Higher concentrations can be achieved without danger of systemic toxicity. 3. High tissue oxygen tension is obtained by the use of a bubble oxygenator in the circuit; the increased oxygen tension has been reported to potentiate the action of x-rays, to which the alkylating drugs have many similarities. 4. Due to confinement of the agent, the host-tumor relationship is relatively undisturbed. The results of animal experiments and the detailed techniques utilized in perfusing various regions and organs in the human have been reported on previously.

The authors treated 33 patients with malignant melanoma with isolation-perfusion techniques. In 24 patients the melanoma involved the lower extremity. The technique for this type of perfusion is described. After exposing the femoral vessels through an oblique incision, below and parallel to the inguinal ligament, heparin is administered intravenously in a dose of 2 mg. per kilogram of body weight. Through a longitudinal incision, plastic catheters are inserted into the femoral vessels and secured by tapes. These are attached to an extracorporeal circuit consisting of 2 sigma-motor pumps and a disposable plastic bag oxygenator. The circuit is primed with 500 to 800 cc. of heparinized blood, and perfusion is begun. A tourniquet, fashioned from ½-in. latex rubber tubing, is then drawn tightly about the extremity above the site of vascular cannulation to isolate the limb from the body. After a well-oxygenated, balanced flow is obtained, the cancericidal drug is injected proximal to the arterial pump head to insure adequate mixing and to prevent streaming. Perfusion is carried out for 20 to 50 minutes, depending on the duration of action of the chemotherapeutic agent. If long-acting agents, such as phenylalanine mustard (PAM) and triethylene thiophosphoramide (TEPA), are used in amounts exceeding the safe total body dose, the extremity is washed out with 500 cc. of fresh blood or dextran at the completion of perfusion. The rubber tourniquet above the site of cannulation is released, the cannulas are removed, and the incisions in the artery and vein are repaired; the heparin is neutralized, and the wound is closed.

In 4 of the 33 patients the perfusion technique was used in conjunction with standard surgical therapy, and in the remaining 29 patients perfusion was for palliation. Four patients have died, 2 of distant disease and 2 as a result of therapy. The disease is controlled or quiescent in 15 patients. The first patient was perfused with PAM in June, 1957, and has shown regression of his lesions. The leg appears free of disease. The results obtained in these cases suggest that isolation-perfusion techniques should be employed with standard surgical therapy in the control of malignant melanoma.

Intracapsular Fractures of the Femoral Neck: Comminution of the Posterior Neck Cortex as a Cause of Unstable Fixation. M. Scheck. J. Bone & Joint Surg. 41-A:1187-1200 (Oct.) 1959 [Boston].

The author points out that, in adduction types of intracapsular fractures of the neck of the femur, nonunion has been reported in a considerable percentage of patients treated by internal fixation. Fracture fragments sometimes become displaced during the postoperative period, despite a satisfactory reduction of the fracture and correct positioning of the pin. This instability has been attributed to the obliquity or vertical inclination of the plane of the fracture, as emphasized by Pauwels. The frequent occurrence of butterfly fragments of cortical bone on the posterior aspect of the neck, along with the displacement of the fragments as seen on lateral roentgenograms, led the author to believe that the obliquity of the fracture described by Pauwels might not be the only cause of instability. Hence, his attention was directed to the cortical bone fragments as an additional factor leading to instability in certain instances. The comminution which occurs on the posterior aspect of the neck is believed to be caused by compression.

The author studied the roentgenograms of 100 randomly selected patients with recent intracapsular fractures of the neck of the femur, but the 14 who were treated by subtrochanteric osteotomy or insertion of a prosthesis were not included in this study. Sixty-nine of the remaining 86 patients who were treated by reduction and pinning were followed. In 59 of these patients, closed reduction and pinning and in 10, open reduction and pinning were done. The follow-up was limited to the study of roentgenograms, because roentgenographic evidence of union or nonunion was considered to be the most important criterion for the evaluation of the factors involved.

Sixty fractures with adequate internal fixation and follow-up were considered suitable for the study of the effect of fragmentation and compression of the posterior aspect of the neck on the stability of the fragments after reduction and internal fixation. A well-placed pin did not prevent the head from settling posteriorly in 21 of these 60 fractures. In 15 of the 21 fractures there was major comminution of the cortex on the posterior aspect of the femoral neck, as seen in the lateral roentgenograms, and in the remaining 6 it is believed that compression of cancellous bone was responsible for the posterior shift of the head fragment. Compression and fragmentation of the posterior cortex of the neck were important factors leading to instability. Compression and fragmentation, alone or in combination with other well-established factors, caused unstable internal fixation and nonunion in 11 of the 16 fractures in which reduction and pinning had been considered satisfactory. Overreduction with the head in a valgus position by the method of McElvenny was a stabilizing factor, which in 9 fractures counteracted the adverse effect of compression and fragmentation of the cortex of the posterior aspect of the neck. The combination of compression and fragmentation of the posterior aspect of the neck with other instability factors, such as a vertical or an oblique plane of the fracture (Pauwels' type 3) or comminution of the inferior aspect of the neck, was responsible for nonunion in 6 of the 16 fractures in which the initial treatment appeared adequate.

NEUROLOGY & PSYCHIATRY

Arterial Hypertension After Poliomyelitis. I. Zimanyi, M. Prohaszka, M. Szondy and S. Ormai. Acta med. scandinav. 164:497-505 (no. 6) 1959 (In English) [Stockholm].

The authors studied over a period of 18 months the occurrence of hypertension in 336 patients with postpoliomyelitic conditions at the Heine-Medin Rehabilitation Hospital and Polyclinic, Budapest. Fifty-three per cent were boys, and 47% were girls, ranging in age from 4 months to 19 years. Of the 336 patients, poliomyelitis developed in 223 in 1957 and in the remaining 113 before that year. The study revealed that 88 (26%) of the 336 patients had hypertension. Mean systolic pressure was increased by 12 to 28%; mean diastolic was 13 to 39% higher than normal values (measured with a standard deviation of 2 sigma). There was no substantial difference in the incidence of hypertension between the 223 patients who had acute poliomyelitis in 1957 (60 patients) and the 113 patients who had acute poliomyelitis earlier (28 patients). Of those affected in 1957, 48% showed a decrease or normalization of blood pressure within one year, but in 52% the hypertension remained, with or without fluctuations. In the other group of 28 patients with hypertension, acute poliomyelitis had preceded the authors' observation by 3 to 13 years, indicating that the postpoliomyelitic hypertension was not transient in nature.

The incidence of hypertension was related to the extent of paralysis: the more extensive the paralysis, the more frequent was hypertension. Hypertension occurred 4 times more often in patients in whom treatment for respiratory insufficiency had to be instituted during the acute phase of poliomyelitis. The incidence of hypertension was twice as great in the encephalobulbospinal form as it was in the purely spinal form. Postpoliomyelitic hypertension is a symptom which should be considered seriously, not only because of its frequent incidence but also because of the complications it may cause. Research in this field may also yield evidence as to the true nature of hypertension of unknown origin occurring in young and adult persons. It should be borne in mind that infections due to enteric cytopathogenic human orphan (ECHO) virus or to Coxsackie virus may have similar sequelae.

Tick-Borne Meningoencephalitis in Sweden. B. Holmgren, J. Lindahl, G. Zeipel and A. Svedmyr. Acta med. scandinav. 164:507-522 (no. 6) 1959 [Stockholm].

During the summer and fall of 1956, 176 patients with diseases involving the central nervous system, such as aseptic meningitis, meningoencephalitis, or poliomyelitis, were hospitalized at the Hospital for Infectious Diseases in Stockholm. Tests made on serum from the 176 patients showed neutralizing antibodies and complement-fixing antibodies to Russian spring-summer/louping ill virus in 68 patients. Thirty of these 68 patients produced significant rise in antibody titer against tick-borne virus in convalescent serum specimens, whereas the remaining 38 had initially a high antibody level, but showed no increase in the antibody titer in the convalescent serum. It is suggested that many of the patients who had no significant rise in the antibody titer, particularly those who had low antibody levels in convalescent serum specimens, had an infection with a tick-borne virus some time prior to the current disease. The clinical data for these 68 patients were similar to those for patients previously observed in European Russia and Central Europe. The disease was characterized by a biphasic course in 70% of the patients. Clinical signs of encephalitis, such as tremor, vertigo, incoordinated gait, mental imbalance, and disturbance of sleep, occurred in about half of the patients. Electrocardiographic examinations showed signs of cerebral dysfunction in 70%, and transient paralyses were found in 25% (6 paralyses of the cranial nerves, 7 paralyses of the spinal nerves involving the shoulder or the upper arm, and 3 paralyses of the bladder or the intestines). The convalescence of the patients was long, lasting from 2 to 14 months.

PEDIATRICS

Staphylococcal Pneumonia in Children: A Review of 83 Cases. R. Koch, M. J. Carson and G. Donnell. J. Pediat. 55:473-480 (Oct.) 1959 [St. Louis].

This report is concerned with 83 patients admitted with staphylococcic pneumonia to Los Angeles Children's Hospital from 1944 to 1958. The diagnosis was based on clinical and roentgenographic evidence of pneumonia, associated with either pyopneumothorax or the isolation of the organism from blood or empyema fluid. Cases of pneumonia with only nasopharyngeal cultures yielding staphylococci, but without either pneumothorax or empyema, were excluded from this study. The fact that 70 of the cases were observed in the 3 years from 1956 to 1958 shows that there has been a great increase in staphylococcic pneumonia in recent years. In 10 children the pneumonia developed while they received hospital treatment for other disorders. Two siblings were affected in each of 3 families; 3 patients were children of physicians; 10 had staphylococcic infection in their families. Measles preceded the onset of pneumonia in 3 patients, and chickenpox in 1. Sixty-one patients were under 1 year of age, and all but 1 of the 10 deaths occurred in infants less than 4 months of age.

Bacitracin, chloramphenicol, erythromycin, oleandomycin, and novobiocin were valuable agents for treatment. Bacitracin with one other effective antibiotic resulted in an improved clinical course and a lower mortality rate. Closed catheter drainage was used when empyema or pyopneumothorax occurred. Rib resection was necessary when drainage was inadequate; decortication of the lung was generally reserved for patients with persistent atelectasis. Long-continuing pulmonary abscess was seen in the right middle lobe in 3 patients who responded to lobectomy. The danger of superimposed infection due to Pseudomonas organisms is emphasized. Polymyxin with either streptomycin or oxytetracycline is the treatment of choice for this complication.

Hemolytic Disease of the Newborn: A Survey of 91 Cases. H. Sonnenschein and N. D. Ritz. Arch. Pediat. 76:387-395 (Oct.) 1959 [New York].

The authors summarize their experience with hemolytic disease of the newborn at the Maimonides Hospital of Brooklyn during a period from Jan. 1, 1956, to Jan. 1, 1958. Studies were made on all women admitted to the obstetric service, including private and ward patients. In the 2-year period a total of 7,202 women were delivered, and erythroblastosis was diagnosed in 91 babies, including one set of twins. During the first 14 months of the study period, the major blood groups were not determined in all the women, but the Rh groupings are complete for the year 1957. The high incidence of Rh-positive patients can be explained by a predominantly Jewish population in this area plus a liberal sprinkling of Puerto Ricans. Both of these groups are known to have a higher percentage of Rh-positive reactors. No significantly increased incidence of group O or Rh-negative mothers was observed in this group. In the beginning the authors had the impression that many patients with *mild* erythroblastosis were being diagnosed as having physiological jaundice, this diagnosis being made in a total of 264 patients.

Eight of the 90 women had a history of erythroblastosis in previous offspring. Such a history proved important in determining severity and prognosis.

The A blood group factor appeared to be a more potent sensitizing agent in a group O mother than the B factor. A cord bilirubin level of 4 mg. per 100 cc. or above in this series was followed by an exchange transfusion in 94% of the cases, whereas other observers suggested that a cord bilirubin level above 5 mg. per 100 cc. makes exchange transfusion almost mandatory. A total of 53 of 91 infants with erythroblastosis received exchange transfusion. There was one fatality due to kernicterus. Almost 50% of 41 cases of O-AB hemolytic disease required exchange transfusion. Only a rough correlation existed between the height of the maternal antibody titer and the severity of the hemolytic disease in the baby.

Prognosis of Lipid Nephrosis Treated by a Prolonged Cyclic Steroid Therapy: Considerations on 41 Patients Treated at the Pediatric Clinic of the University of Modena During 6 Years. R. Pachioli, E. Cheli and E. Lavaga. Arch. franç. pédiat. 16:776-779 (no. 6) 1959 (In French) [Paris].

The authors used steroid drugs in the treatment of 30 boys and 11 girls, aged 18 months to 12 years, with lipid nephrosis. The daily dose level of the steroids per kilogram of body weight was as follows: corticotropin (ACTH), 5 to 8 units when administered intramuscularly and 1 or 2 units when administered intravenously; prednisone or prednisolone, 2 or 3 mg.; and dexamethasone, 0.2 mg. The therapy was cyclic, the periods ranging from 8 to 12 days at the beginning and later from 3 to 6 days. The drug-free intervals extended from 4 to 10 days. Remission of symptoms has been observed in 34 patients, having lasted from 3 months to 2 years in 10 patients and from 2 to 5½ years in 12; 12 patients are still hospitalized with a slight degree of proteinuria. Two patients derived no benefit from the treatment, and 5 patients died—2 of bronchopneumonia and 3 of renal insufficiency. Recurrence took place in 6 patients; 3 of these patients recovered completely, 2 have a slight degree of proteinuria, and 1 died. A slight degree of transitory albuminuria not accompanied by clinical symptoms was observed in 5 patients. There were no severe complications related to either the high dose level or the prolonged treatment. A mild variety of adrenocortical obesity frequently developed, but it disappeared within 2 months after discontinuance of treatment or by instituting brief courses of treatment in combination with long drug-free periods.

The authors conclude that ACTH seemed to exhibit more rapid therapeutic action than other steroids. ACTH also was effective in some patients who had been refractory to other steroids. Prednisone and prednisolone had a slower action but produced less edema, and have been used for maintenance treatment.

Congenital Neurocutaneous Syndromes in Childhood: II. Tuberous Sclerosis. D. Hsi-Chih Chao. J. Pediat. 55:447-459 (Oct.) 1959 [St. Louis].

At the Blue Bird Circle Children's Clinic, Texas Medical Center in Houston, 8 patients with tuberous sclerosis have been observed since 1951. On the basis of these 8 cases and of literature reports, the author discusses various aspects of tuberous sclerosis. A triad of symptoms, consisting of epilepsy, mental deficiency, and adenoma sebaceum, is seen in fully developed cases of tuberous sclerosis. Any phase of the triad may be manifest alone, or any two may occur in the absence of the third. The etiological diagnosis is often overlooked in the early stage when seizures are the only symptoms. Seizures were the chief complaint in all 8 children. The diagnosis of tuberous sclerosis was readily made in 2 patients in whom the classical clinical picture was present. In the other 6 children the etiological diagnosis was not made until adenoma sebaceum developed during observation. In retrospect, however, a variety of other cutaneous manifestations, such as depigmented areas, café au lait spots, plaques, etc., had been noted before the appearance of the characteristic facial lesions. These earlier skin changes should, therefore, arouse suspicion of tuberous sclerosis.

Tuberous sclerosis is a developmental anomaly. In the same family some persons may exhibit the typical clinical picture, while others have rudimentary or incomplete manifestations, e. g., epilepsy, adenoma sebaceum, retinal tumors, and renal tumors, alone or in various combinations. The anatomic changes begin early in embryonic life. Although it does not seem likely that new foci of disease develop after birth, preformed foci may not become manifest for some time after birth, at puberty or even later. In the brain the lesions of tuberous sclerosis are smooth, hard, white nodules. The skin lesions are nevoid in character and consist mainly of hyperplastic connective and vascular tissue (fibroangiomatous nevi). Visceral abnormalities which may coexist are fibroadenoma of the kidney, rhabdomyoma of the heart, and cystic defects of the lungs and of the skeletal system.

Two types of adenoma sebaceum are commonly seen in tuberous sclerosis: the red, seed-like spots and the nodular form with the color of normal skin. In the series presented, only one patient had typical sebaceous adenoma lesions. In 6 patients the facial lesions developed subsequent to the initial visit. Five of the 6 patients had the red, seed-like type of adenoma sebaceum initially. Several of the patients had plaques. Subungual fibroma was observed in one patient. Depigmented patches (areas of vitiligo) were more common than café au lait spots. The family history was largely negative for neurocutaneous syndromes. In only one case was there a positive family incidence, the father having the subcutaneous nodular type of neurofibromatosis and a younger brother having a few café au lait spots on the body and a small cavernous hemangioma on the shoulder.

The treatment must be adjusted to the individual patient. It must take into account the mental and behavioral changes and the severity of the seizures. Patients with the mild form may make an adequate social adjustment and be cared for at home. Marked mental deficiency may necessitate custodial care. The treatment of seizures with anticonvulsant drugs is often only partially effective. The patient with the fully developed aspects of tuberous sclerosis rarely lives beyond the age of 25 years. The life expectancy depends on the location and extent of the disease in the central nervous system. Status epilepticus or intercurrent disease is often the immediate cause of death. Cardiac and renal involvement has occasionally been responsible for death in adults but has not been reported in children.

Ovarian Tumors in Childhood: Report of Six New Cases and Review of the Literature. H. Characke. A. M. A. Arch. Surg. 79:573-580 (Oct.) 1959 [Chicago].

The author reports on 6 girls, between the ages of 2 and 15 years, with ovarian tumors; 1 patient had a malignant teratoma of the right ovary with intra-abdominal metastasis and spontaneous regression, 1 had bilateral malignant dysgerminoma, 2 had bilateral carcinoma of the ovaries with abdominal metastasis, 1 had carcinoma of the left ovary with abdominal metastasis, and 1 had a fibroma of the left ovary with myxomatous changes and calcification. Observations on these patients, and in 257 cases of ovarian tumors in children collected from the literature, revealed as the chief complaint a history of progressive abdominal enlargement, abdominal mass, and abdominal pain. The pain is increased during periods of activity. It may be excruciating when there is torsion of the tumor pedicle, and may be associated with nausea, vomiting, high temperature, and high white blood cell count, giving the clinical picture of an acute surgical condition within the abdomen, including acute appendicitis. Pressure of the tumor on the ureters, bladder, and intestine may result in disturbance of urination and defecation. In some patients in whom the tumor fills the abdomen, or in the presence of ascites, there may be digestive and respiratory disturbance.

The treatment of choice for ovarian tumor in infants and children is exploratory laparotomy. When the tumor is found to be unilateral with an intact capsule, without involvement of any other abdominal structure, conservative surgical intervention, a unilateral salpingo-oophorectomy, will suffice, care being taken to prevent rupture of the capsule of the tumor, with escape of its contents into the peritoneal cavity. Irradiation therapy should be withheld, except in patients with dysgerminoma, in whom sterility is common even without irradiation and the tumor is radiosensitive. Radical surgery followed by irradiation therapy is indicated if the tumor is bilateral or if a frozen section of the removed tumor proves it to be highly malignant regardless of the type. Irradiation therapy alone, chemotherapy, and hormone therapy are reserved for malignant tumors with widespread metastasis. The prognosis of ovarian tumors in children depends on the degree of malignancy of the tumor, whether it is unilateral or bilateral, and whether regional or distant metastasis has already taken place. Of the 6 patients, the girl with malignant teratoma survived for 13 years, the patient with bilateral malignant dysgerminoma was lost to follow-up, the 3 patients with carcinoma died, and the patient with fibroma made an uneventful recovery after the surgical removal of the tumor.

Ovarian tumors in children are not frequently seen. Such a possibility is seldom considered in a differential diagnosis of "abdominal mass." A good history alone may be suggestive enough to warrant a preliminary diagnosis of a "possible ovarian tumor." In most cases the uterus and its appendages are practically abdominal organs in infancy, or the ovarian tumor may extend into the abdomen by a long pedicle. Hypertrophied breasts and sex organs, vaginal discharge or bleeding, mature appearance of the infant or child, or pseudohermaphroditism will all further suggest ovarian tumor. Abdominal palpation may reveal the presence of a mass which may be the size of an orange, or may fill the entire abdomen, or it may not be felt at all. A flat plate of the abdomen may show a dense, soft-tissue shadow of the tumor. Chest roentgenograms should be taken in all patients with ovarian tumors to detect metastasis or Meigs's syndrome. A moderate increase of 17-ketosteroids and an enormous increase of estrogen may be revealed by laboratory findings.

The Blood Volume of Infants: II. The Premature Infant During the First Year of Life. T. R. C. Sisson, L. E. Whalen and A. Telek. J. Pediat. 55:430-446 (Oct.) 1959 [St. Louis].

The authors studied the blood plasma and erythrocyte volumes and the total circulating hemoglobin mass of premature infants from birth through the first year of life. The subjects of this investigation were 51 premature infants in good condition, on whom 145 plasma volume determinations were performed. Six serial observations were made of 1 infant, 5 of 8 infants, 4 of 9, 3 of 10, 2 of another 10, and a single observation of 13 infants. The average blood volume at birth was found to be 109 ml. per kilogram, a value slightly higher than in full-term infants. In the first 2½ months of life there was a tendency for the plasma volume to increase as the erythrocyte volume decreased. This had the effect of maintaining the total blood volume at a relatively high level. The erythrocite volume at birth was 45.5 ml. per kilogram (about 5 ml. higher than in full-term infants) and was close to 20 ml. per kilogram between 12 and 52 weeks of age. There was no significant correlation between erythrocyte volume and growth gain, or between erythrocyte volume and venous hematocrit. Normal growth increments far outdistanced the expansion of erythrocyte volume.

The circulating hemoglobin mass was 36.5 Gm. in the first 2 days of life; it declined 33% by 4 weeks of age. At 12 weeks it was again at the value recorded in the first 2 days. Further increments were more gradual. On the basis of body weight, there was an abrupt fall from 20.5 Gm. per kilogram at birth to 10 Gm. at 6 weeks. The average value remained between 6.4 and 8 Gm. per kilogram for the rest of the year. There was poor correlation between the values for hemoglobin concentration and circulating hemoglobin mass in both the neonatal period and later. The total hemoglobin iron reached its lowest level between the 3rd and 6th weeks of life. By the 10th week, values recorded in the 1st week were regained. It was concluded that erythropoiesis became active between 3 and 7 weeks after birth and that the original iron stores were adequate for hemoglobin synthesis until only about 10 weeks after birth. This explains in part the development of iron depletion and iron deficiency at an earlier age in the premature infant than in the full-term one.

The authors conclude that, within the limitations of the techniques used, the values reported are representative of an urban clinic group. Considerable variation about the mean values was present throughout the year. The average values, therefore, indicate changes that may be expected in the first year of life but should be considered specific in only a restricted sense.

Nutritional Performance of Linseed-Oil Containing Formula in Suckling Infants: Clinical-Statistical Observations with Improved Method. J. Jochims. Monatsschr. Kinderh. 107:397-402 (Sept.) 1959 (In German) [Berlin].

The author performed comparative nutritional experiments, in an alternating series, on 622 suckling infants in the course of the first 6 months of their lives. Three hundred thirty-four infants received a normal, two-thirds acid milk, and the other 288 received a milk in which the butter fat had been substituted by linseed oil. The average duration of the experiment in the first group of infants was 32.5 days, and in the second group it was 31 days. For the evaluation of the results 5 criteria were employed, namely, increase in body weight, new attacks of dyspepsia in the course of the nutritional trial, tendency to infection, usefulness of the formula for treatment of dyspepsia, and tolerance of an occasional oversupply of food. The increase in body weight was practically the same in both groups of infants. In contrast to that, the formula containing linseed oil definitely increased the tendency to dyspepsia in the infants; this was manifested by an increased occurrence of mild dyspepsia. A more detailed analysis showed that this increased incidence of dyspepsia did not result from bacterial infection of the intestines and was hardly elicited "parenterally," i. e., by respiratory infections. The observed disturbances were apparently of an alimentary nature, and they were mild. The linseed oil, therefore, does not seem to be as well tolerated as the butter fat by highly sensitive suckling infants.

Clinical Experiences with the Activity of Novobiocin as a Growth Factor. A. Verga. Minerva pediat. 11:870-873 (Sept. 8) 1959 (In Italian) [Turin, Italy].

Novobiocin as a growth factor was experimented with in 38 premature infants, aged above 30 days. The treatment lasted between 5 and 13 days. The daily doses were below the therapeutic level; they consisted at first of 25 mg., but were subsequently reduced to 10 mg. Diet and prophylactic treatment were carried on unchanged simultaneously with the specific treatment. Body growth increased considerably in 33 infants. The daily gain in weight was more than 30 Gm. in 14. The gain in weight was noted in most instances from the first day of treatment and gradually increased. Daily gain in weight in some instances reached peak values of from 60 to 70 Gm. Improvement in general state of health and in condition of the skin invariably accompanied the improvement in body growth. Body growth was followed up in 30 infants after discontinuance of the treatment with novobiocin; it continued well in 15 infants until discharge, but a diminished rate or complete arrest of body growth was observed in 15 infants. Treatment with novobiocin was repeated in 3 infants. A new increase of body growth, but at a slower rate than during the first course of treatment, was observed. This study demonstrates that stimulation of the body growth of premature infants is one of the activities of novobiocin.

DERMATOLOGY

Evaluation of Treatment of Warts by Hypnosis. A. H. C. Sinclair-Gieben and D. Chalmers. Lancet 2:480-482 (Oct. 3) 1959 [London].

The authors report on 14 patients, all of whom had bilateral, multiple common warts of at least 6 months' duration and who were treated by hypnosis. It was suggested to the patients that the warts on one side of the body (the side that had more or larger warts) would disappear. In 9 of the 10 patients in whom deep or moderate hypnosis was achieved, the warts on the "treated" side disappeared, while those on the control side remained unchanged. This treatment was effective in all patients who were hypnotized deeply enough to perform, on awakening, some action that had been suggested to them. Hypnotic suggestion confined to one side of the body could prove a useful means of investigating the causation of various conditions.

The Emotional Factor in Psoriasis. W. Susskind and R. J. McGuire. Scottish M. J. 4:503-507 (Oct.) 1959 [Glasgow].

Psoriasis accounts for approximately 6% of all cutaneous disorders. Periodic relapses are common, the etiology is as yet uncertain, and there is no permanent remedy. The authors describe a pilot study on 20 patients. In addition to routine dermatological examination, the patients were interviewed, and detailed material was obtained relative to possible parallelism between the cutaneous manifestations and disturbing life-events. Stressful life-situations involving the mobilization of severe anxiety and unexpressed resentment occurred in relation to the onset of the disease in 8 cases and in association with exacerbations in 14 cases.

As this was a pilot study without a control group, there is a possibility that the association is merely the spurious product of diligent history taking or, if a real one, not specific to psoriasis. Since many of the life-events were accompanied not only by an outbreak of psoriasis but also by affective disturbance, the association is more likely to be a meaningful one. The provocative situations tended to have qualitative features in common. With respect to the onset of psoriasis, the disturbing events among the 8 patients in question were largely of an acute catastrophic nature, e. g., illness or death of a relative, break-up of marriage, etc. The patients became insecure and experienced feelings of personal loss, often coupled with unexpressed resentment. A similar psychodynamic pattern was evident in the 14 patients in whom relapses of psoriasis were associated with emotionally charged events. This psychodynamic background closely resembles that seen in depressive states. The analogy with depressive states is further highlighted by Tommasi's (1947) finding that in 4 psoriatic patients electroshock therapy was successful in clearing the eruption without any local treatment in 2 cases. The possible association with affective disorders merits more thorough investigation.

Use of Griseofulvin in the Therapy of Tinea Capitis in Children: Preliminary Observations. J. Kirk and L. Ajello. A. M. A. Arch. Dermat. 80:259-267 (Sept.) 1959 [Chicago].

For a number of years the District of Columbia's Department of Public Health has been contending with tinea capitis infections among school children and their preschool siblings. In 1956, 1,766 cases were seen. The authors report on the treatment of this infection with the antibiotic griseofulvin and on the results obtained with various doses of this drug in 81 cases. The infection was caused by Microsporum audouini, M. canis, and Trichophyton tonsurans. Griseofulvin appears to be a specific agent against the invasion of newly formed hair by these fungi. Normal hair growth may be noted in 3 weeks, but a few faintly green-fluorescent hairs have been present for as long as 8 weeks in Microsporum infections, with fungus-bearing stubs, scales, and debris remaining for as long as 95 days under continuous therapy. As the infected portion of the hair grows, this must be cut off. Clipping or shaving of the hair from the affected areas is advised, beginning on or before the 21st day of treatment, and should be continued until cure is obtained. Scrupulous cleanliness has seemed to facilitate the removal of infectious scales and debris. Because of the recurrence of lesions after a single negative culture in 3 patients treated with low dosages and for 4 weeks or less, the authors suggest that treatment be maintained until 2 cultures taken at one-week intervals are negative and that a third culture 2 weeks after treatment is ended be negative before the patient is discharged as cured. Wood's-light examinations should be continued for a minimum of one month after therapy is completed.

Of 13 patients with M. audouini infection treated from 28 to 70 days with dosages of griseofulvin ranging from 10.0 to 17.4 mg. per pound per day, 10 were Wood's-light negative by the 28th day of treatment and 2 by the 42nd day of treatment. One patient who stopped treatment at the 28th day still had Wood's-light-fluorescent hairs 2 weeks later. Of this group, 10 had begun to show consistently negative cultures by the 70th day of observation, 2 remaining culture-positive after 77 days of continuous therapy. Although M. canis and T. tonsurans infections have responded to griseofulvin therapy, the series presented is too small for conclusions as to optimum dosage. Therapy was uniformly more successful in the T. tonsurans group in the dosages used. Of 120 patients on griseofulvin therapy, periorbital edema in 2 cases has been the only untoward reaction noted.

An Epidemic of Infectious Erythema in Germany. H. Grimmer and A. Joseph. A. M. A. Arch. Dermat. 80:283-285 (Sept.) 1959 [Chicago].

By the end of October, 1958, there occurred in Berlin an outbreak of an apparently new skin eruption which soon exploded into epidemic proportions. The condition was soon discovered to be identical with erythema infectiosum. The authors report on 200 patients observed within a month's period at the skin clinic of the Free University of Berlin. There were twice as many women as men; adolescents and middle-aged people were more affected; the oldest patient seen was an 81-year-old man. The incubation period seemed to fluctuate from 5 or 6 days to 2 weeks. The exanthem appeared overnight without premonitory symptoms. Occasionally some patients reported that they had noticed signs of a head cold or sore throat prior to onset. There was no fever, sometimes elevated temperature, no enlargement of the lymph nodes, and no malaise, as far as the milder cases were concerned. These resembled measles and rubeola, presenting a rosy-red maculopapular eruption, beginning on hands and arms, also on the face, and rapidly spreading to the trunk and lower extremities, including the soles. As more people became affected, the rash assumed a bizarre and polymorphous appearance. Even in the same person it varied from a morbilliform distribution on face and limbs to huge coalescent patches of a bright red hue, covering the greater part of the body surface, sometimes changing to hemorrhagic lesions, especially on the legs. The blood picture was not characteristic. The histopathology studied in 10 cases was that expected in an acute erythema, showing the signs of an exudative process. There was edema, dilatation of the blood vessels, with perivascular infiltration consisting of lymphocytes with occasional plasma cells. The infection was always self-limited and cleared after from 4 to 20 days. Relapses occurred after a free interval of 8 to 10 days in a few cases. The treatment was symptomatic and consisted of high fluid intake, large doses of ascorbic acid, calcium, antihistaminics, and antipruritic lotions. Corticosteroids were administered in severe cases.

THERAPEUTICS

The Response of 306 Pulmonary Tuberculous Cavities to Chemotherapy. P. Puech, J. Hardre, C. Ackermann and J. L. Simonin. Rev. tuberc. 23:685-702 (July) 1959 (In French) [Paris].

Between January, 1954, and December, 1957, 265 students with pulmonary tuberculosis, ranging in age from 18 to 30 years, presenting 306 cavities, were admitted to the sanatorium for students in Saint-Hilaire-du-Touvet. Of these 265 patients, 241 had 1 cavity, 29 had 2 cavities (homolateral in 5, bilateral in 24), 1 had 3 cavities, and 1 had 4 cavities. Patients who were subjected to collapse therapy, or in whom surgical removal of the pulmonary lesion was performed, or who were lost for follow-up were not included in this study. Isoniazid was routinely administered in daily doses ranging from 0.30 to 0.40 Gm. to all patients; this drug was combined with PAS, given either intravenously or by mouth to 25% of the patients; it was combined with streptomycin and given to 75% of the patients; after withdrawal of streptomycin, isoniazid was administered with PAS. The duration of treatment varied from 9 to 24 months. Serial chest roentgenograms made throughout the treatment and during the follow-up for 2 years showed closure of cavities in 78% of the patients. After 9 months of treatment, however, 35.9% of the cavities persisted, but improvement of the pulmonary lesions was obtained during the following months with antibiotics and bed rest.

This study showed that the roentgenologic aspect of cavities (location, size, associated lesions), at the initial stage of the pulmonary disease, does not influence the final results. Older lesions or previous treatment do not inhibit the healing of cavities; they merely delay the disappearance of cavities. Healing of the cavities depends on the rapid destruction of Mycobacterium tuberculosis. and this. in turn, can generally be achieved by the initial treatment. The importance of immediate and vigorous initial treatment during the first 2 months of the disease was shown by this study. The fate of the patient with cavities and, in general, of all those with tuberculosis is determined in the first months of treatment.

Pyrazinamide in the Treatment of Tuberculous Meningitis in the Adult: A Report on Observations Made on 18 Patients. C. Mauro and G. Romano Minerva med. 50:2956-2962 (Sept. 19) 1959 (In Italian) [Turin, Italy].

The authors report on the effect of pyrazinamide on 18 patients, most of them adults, with tuberculous meningitis; previously 10 of these patients had been treated with streptomycin. Tablets containing 0.5 Gm. of pyrazinamide each were used. Two tablets (1 Gm. of the drug) were given to each patient on the 1st and the 2nd day of treatment, 4 tablets (2 Gm.) on the 3rd and the 4th day, and 6 tablets (3 Gm.) after the 5th day. The treatment lasted for an average of 40 days. A resolution of symptoms, such as headache, vomiting, rigidity of the neck, and pain in the vertebral column, which persisted even after prolonged treatment with streptomycin and isoniazid, was obtained after an average of 20 days of treatment with pyrazinamide in 5 patients. Recovery of the sensory apparatus was obtained after 20 days of treatment in 2 patients. Fever subsided gradually on treatment with pyrazinamide. Progressive improvement of strabismus was observed in 3 patients, and resolution of it in one patient, after 30 days of treatment. Resolution of other symptoms, such as psychomotor agitation and vertigo, was obtained in some patients after 15 to 40 days of treatment. One patient, on the 4th day of treatment, suffered from toxic effect of the drug on the liver; his condition, however, returned to normal as soon as the drug was withdrawn. Three of the 18 patients died, 1 of bulbar paralysis and 2 of deterioration of their general condition.

Pyrazinamide caused marked changes in the blood picture of most patients in this series; blood tests became negative in 9 patients, improved in 5, and remained unchanged in 3. Best results were obtained in the patients who before pyrazinamide therapy had been treated with streptomycin. The authors believe that pyrazinamide is most useful in those patients who, although they at first benefited from streptomycin and isoniazid, eventually became resistant to those drugs. Pyrazinamide, however, cannot be a substitute for either streptomycin or isoniazid, and it may be useful if given in combination with these 2 drugs.

New Antituberculotic Preparation: Alpha-Ethyl-*Thioisonicotinamide (TH 1314) in the Treatment* of Pulmonary Tuberculosis. P. Véran, N. Rist, R. Trichereau and others. Presse méd. 67:1597-1600 (Sept. 19) 1959 (In French) [Paris].

A clinical study of the therapeutic value of alpha-ethyl-thioisonicotinamide (TH 1314) was made with 120 tuberculous patients. The average length of the treatment was 7 to 10 months for the patients with tuberculosis of long duration and 4 to 6 months for those with tuberculosis of recent onset. This report covers the results obtained in 38 patients with long-duration tuberculosis, all with cavitation, and in 17 patients with recent lesions. In order to avoid the development of resistance to the drug as far as possible, alpha-ethyl-thioisonicotinamide was never administered alone. To the patients with long-duration tuberculosis it was administered in association with streptomycin (7 cases), aminosalicylic acid (PAS, 14 cases), and cycloserine (17 cases). The dose of streptomycin was 1 Gm. daily or every other day, or every 2 days if the previous total dosage had exceeded 80 Gm.; PAS was administered in daily perfusions whenever possible; and cycloserine was given in doses of 0.5 to 1 mg. daily. One tablet of alpha-ethyl-thioisonicotinamide (0.25 Gm.) was given twice a day, after the main meals. Depending on the degree of individual tolerance to the drug, the dose limit was 1 Gm. daily for patients weighing 60 kg. (132 lb.) or more, and 0.50 to 0.75 Gm. for those weighing less than 60 kg. After 8 months of observation alpha-ethyl-thioisonicotinamide was administered in the form of suppositories, which were much better tolerated and allowed increasing the daily dose to 1.5 Gm.

Clinically, the effects of TH 1314 therapy were especially noticeable in relieving symptoms, such as fever and cough, although the patients did not experience the euphoric feeling of general improvement which is obtained with isoniazid (INH). Of the 17 patients with recent tuberculosis who were treated during 3 to 6 months with alpha-ethyl-thioisonicotinamide combined with either streptomycin or cycloserine, 5 recovered, 6 experienced good improvement, and 3 had fairly satisfactory improvement. Of 19 patients with old lesions and in rather serious condition, 2 recovered, 8 obtained good improvement, and 2 had a fair degree of improvement. Of the other 19 patients with old tuberculous lesions, who were in critical condition, none recovered. As evidenced by roentgenograms, good results were obtained in 65% of the patients with recent lesions, in 52% of those with old lesions and moderately grave condition, and in 5% of the critically ill. The causes of failure in 34 patients are discussed and attributed to 2 facts, namely, association of alpha-ethyl-thioisonicotinamide with only one other drug, instead of 2, and insufficient dosage of viomycin.

The results show that alpha-ethyl-thioisonicotinamide is an excellent drug for an attack against tuberculosis and can be combined with or replace isoniazid when resistance to the latter has developed. When it is well tolerated, it can replace streptomycin or PAS during the triple therapy which is so beneficial to patients with recent tuberculosis. To patients with long-duration tuberculosis alpha-ethyl-thioisonicotinamide should be given in association with 2 new drugs (cycloserine and viomycin, or kanamycin, are recommended). When surgical therapy is advised, treatment with TH 1314 for 6 to 16 weeks, if well tolerated, may create the best possible condition for the operation. If there is resistance or intolerance to a previously combined therapy, the preoperative treatment should be limited to 2 or 3 weeks, and the administration of alpha-ethyl-thioisonicotinamide should aim especially at reinforcement of the postoperative treatment.

Chlorpropamide in the Therapy of Diabetes Mellitus: First Clinical Observations. A. Vitelli, C. Mattei Grandis, A. M. D'Urso and F. Siracusa. Minerva med. 50:2856-2859 (Sept. 12) 1959 (In Italian) [Turin, Italy].

The authors report a study on the effect of chlorpropamide, a new hypoglycemic drug, which was given orally to 24 patients, 40 to 75 years of age, 10 with mild diabetes and 14 with moderate diabetes. One patient had suffered from diabetes since youth, and the others since after their 40th year of life. Diabetes had been present for more than 5 years in 7 patients, for 2 to 5 years in 5, and for less than 2 years in the remaining patients. The daily intake of carbohydrates was reduced to 180 to 200 Gm. 5 days before the administration of the drug and throughout the treatment. The patients with mild diabetes received chlorpropamide in a beginning dose of 0.25 Gm. to 1 Gm. per day and a maintenance dose of 0.25 to 0.75 Gm. per day; the patients with moderate diabetes received a beginning dose of 0.5 Gm. to 1.5 Gm. and a maintenance dose of 0.25 to 1 Gm. per day. The patients were kept under observation for from 20 to 160 days.

Chlorpropamide had a beneficial effect in 23 of the 24 patients of the series. Only the patient who had suffered from diabetes since youth failed to respond to the treatment. The values of glycemia declined and became stabilized at below 150 mg. per 100 cc., and the urine presented no glucose in 10 patients with mild diabetes and in 9 with moderate diabetes. The values of glycemia declined 170 to 180 mg. per 100 cc. and the amount of glucose present in the urine did not exceed 6 to 7% of the total intake of sugar in 3 patients who had suffered from moderate diabetes for [illegible] 5, and 9 years respectively. A satisfactory sugar metabolism was found in 3 patients who after 3 weeks of treatment with chlorpropamide received only dietetic treatment. Some patients were able to alternate periods of treatment with chlorpropamide with periods of only dietetic treatment. The drug which was well tolerated in most instances had to be discontinued in 3 patients because of gastric symptoms. No relevant side-effects were observed during the treatment. A moderate and progressive increase in body weight was observed in all instances.

The authors believe that the optimal dose of chlorpropamide is 0.5 to 1 Gm. for 3 to 7 days, after which it is reduced to 0.125 to 0.75 Gm. They also believe that there is no relationship between the activity of the drug and the duration of the diabetes, the age of the patient at the time treatment is begun, and the amount of insulin given before treatment with chlorpropamide.

Diarrhea Caused by Staphylococcic Enteritis After Intravenous Tetracycline Therapy. P. Lundsgaard-Hansen and A. Senn. Schweiz. med. Wchnschr. 89:985-987 (Sept. 19) 1959 (In German) [Basel, Switzerland].

After general comments on the tetracycline group of antibiotics, the authors mention one of the newer derivatives of this group, which is water-soluble and suitable for intravenous use. It is the pyrrolidinomethyltetracycline, known as Reverin. So far this preparation has been regarded as largely free from risk, particularly with regard to the development of staphylococcic enteritis. The authors present histories of and comments on 6 patients in whom staphylococcic enteritis with severe diarrhea developed during the postoperative phase after the intravenous administration of the aforementioned tetracycline preparation. Although the concentration of tetracycline in the intestinal lumen is much lower after intravenous than after oral administration, it is nevertheless quite adequate to inhibit the normal intestinal flora, and thus to produce favorable conditions for superinfection with staphylococci that are resistant to tetracycline. Although none of the 6 patients died as the result of the postoperative staphylococcic enteritis, their histories demonstrate the urgent need of careful supervision of surgically treated patients who receive intravenous injections of a tetracycline derivative. In an addendum it is pointed out that, since submitting this paper, another case of staphylococcic enteritis, this time fatal, occurred in a 35-year-old man. At autopsy, staphylococcic septicemia was found. The ulcerations seen in the small intestine must be assumed to represent the point of origin of the blood stream infection.

PATHOLOGY

Congenital Aneurysm of the Left Atrium. G. F. Wagman, H. J. Linn and S. E. Gould. A. M. A. Arch. Path. 68:266-274 (Sept.) 1959 [Chicago].

Only one report has been encountered of a congenital cardiac aneurysm or diverticulum of the atrium, exclusive of aneurysm of the septum ovale. This prompted the authors to report on a 69-year-old woman with a large aneurysm of the wall of the left atrium, probably of congenital origin. The aneurysm was situated above the posterior leaflet of the mitral valve, in the area of the left atrium. It is concluded that this aneurysm was caused either by a defect in the musculature of the left atrium at that site or by a defect in attachment of the musculature to the mitral ring. In the area of displacement of the coronary sinus, that portion of the wall of the coronary sinus lying closest to the atrial musculature lacked a coat of cardiac muscle. This may have been caused by a developmental muscular defect or by stripping off of muscle as the outpouching developed. Whether the aneurysm was present at birth or developed subsequently in an area that was predisposed by abnormal muscular development cannot be determined. On the basis of an old healed rheumatic type of mitral valvulitis, acute strain of sufficient intensity to cause outpouching of a congenitally weakened area might be postulated. It is interesting to note that this large thin-walled aneurysm of apparent long duration did not rupture or elicit any cardiac symptoms.

Bronchopulmonary Aspergillosis: Report of Two New Cases, Review of Literature, and Suggestion for Classification. A. F. Naji. A. M. A. Arch. Path. 68:282-291 (Sept.) 1959 [Chicago].

There are 2 kinds of lesions produced by Aspergillus organisms: (1) intracavitary fungous mass or intracavitary aspergilloma, and (2) bronchopneumonic aspergillosis. Twenty patients with the former type and 17 with the latter have been observed, and 2 cases of each type have been reported in detail. The clinical and pathological findings differed greatly in the 2 types of lesions. Fourteen of the 20 patients with intracavitary aspergilloma presented hemoptysis as their main symptoms. Tubercle bacilli were not found in the sputum of any of these patients. Fungous mycelia were noted in 4 patients. An upper lobe was the site of infection in 17 of the 20 patients. The lesion had a roentgenographic appearance characterized by a well-defined oval or circular opacity, or a cavity containing a mass. The pathological findings in the lobe involved were characterized by a cavity lined with bronchial epithelium and containing a loose mass of mycelia, identified as Aspergillus.

Sixteen of the 20 patients were treated successfully by lobectomy or segmental resection; 2 patients died after surgical intervention. The excellent results after lobectomy and the difficulties in arriving at a definite diagnosis on clinical grounds are an indication for a surgical approach in such patients. The lung lesions in the 17 patients with bronchopneumonic aspergillosis were in the form of bronchopneumonia with involvement of more than one lobe. Bilateral distribution was present in 11 of the 17 patients. The roentgenographic appearance was that of a nonspecific pneumonitis. Six of the 17 patients improved after iodide therapy, while the disease was fatal to 10 patients; it became generalized in 4 cases. In 7 of the 17 patients the diagnosis of aspergillosis was made by finding the fungus on direct sputum examination or culture. In the remaining 10 patients the fungus was found at autopsy in the lung lesions.

he Patient as a Source of Nosocomial Staphylococcal Infections. R. Beezy, R. E. Bormes and M. L. Koch. Antibiotic Med. 6:401-406 (July) 1959 [New York].

The authors evaluated 937 patients in the Wood Veterans Administration Hospital in Milwaukee for evidence of clinical and subclinical pyogenic infection on Oct. 20, 1958. This one-day survey of all the patients in a general hospital revealed that 188 (20%) of these patients had evidence of clinical or subclinical pyogenic infection in one or more sites, and 88 (47%) of the 188 patients were proved by culture to have coagulase-positive staphylococci at the site of culture. Thus, on the day of survey the hospital staphylococcic infection rate was 9.4%. Of the 937 patients, 405 were on the medical service and had a staphylococcic infection rate of 4.4%; 332 were on the surgical service and had a staphylococcic infection rate of 10%; and 200 were on the geriatric service and had a staphylococcic infection rate of 18%. Patients on the geriatric and surgical services, with localized subclinical infections associated with a foreign body, were the most frequent source of coagulase-positive staphylococci of a phage pattern usually associated with virulence and drug resistance. Such patients are potentially capable of transmitting disease if strict asepsis is not maintained. As a result of this survey, a program has been established to encourage greater discrimination in the use of available antibiotic agents and to emphasize the importance of the practice of strict aseptic techniques.

The Histological Appearance of Gastrointestinal Polyps in the Peutz-Jeghers Syndrome. A. Rintala. Acta chir. scandinav. 117:366-374 (no. 5) 1959 (In English) [Stockholm].

Numerous cases are on record of familial gastrointestinal polyposis associated with circumoral melanin pigmentation (Peutz-Jeghers syndrome), in which the polyps supposedly had undergone malignant degeneration. The author reviews the literature on the histology of the polyps in the Peutz-Jeghers syndrome and describes the histological appearance of the polyps that were removed from 3 patients (father and 2 daughters) in 8 operations. Polyps of the small intestine were removed in all 3 patients, and in addition gastric and colonic polyps were removed in one and appendical polyps in another.

The polyps of the small intestine show all 3 epithelial cell types of the corresponding area of the intestine arranged mostly as in the normal mucosa. In the large intestine, however, the epithelium of the polyps consists essentially only of goblet cells. The gastric polyps also show at the base the multiple cell types of the corresponding mucosa, although there is a more adenoma-like picture at the periphery, the proliferating surface epithelium being most prominent. The stroma of the polyps, particularly of those in the small intestine, is branched and reticular, and muscle fibers are dispersed among the glandular tissue. This may have been interpreted mistakenly as infiltrative growth.

So far there are only 2 cases of the Peutz-Jeghers syndrome in which the polyps underwent malignant degeneration. In other cases, in which the intestinal polyps have been judged malignant, the diagnosis seems to have been based on an erroneous interpretation of the histological picture. As far as it is known, no patient with the Peutz-Jeghers syndrome has died of carcinoma arising in the polyps of the small intestine, nor have any metastatic lesions been reported in this condition.

Splenomegaly—Early Symptom in Osteomyelofibrotic Syndrome? S. Blom, A. Lindgren and M. Rasch. Nord. med. 62:1419-1421 (Sept. 24) 1959 (In Swedish) [Stockholm].

The case described, in a woman aged 52 years, seemed to be one of aplastic anemia of unknown etiology leading to extramedullary blood formation. In the beginning splenomegaly dominated the picture. There was no evidence of leukemia or collagenosis. The marked hemosiderosis could be explained partly as endogenic due to the anemia, partly the result of the 74 blood transfusions given the patient. Therapeutic possibilities seemed slight. After a few months the initial splenic enlargement was followed by anemia resistant to transfusions and steroid therapy. Splenectomy gave rapid clinical and hematological improvement, but a leukoerythroblastic blood picture and fibrotic changes in the skeleton developed. The patient died 2 years after admission and 1½ years after splenectomy. Eosinophil infiltrations were found in the excised spleen, in the bone and bone marrow on repeated examinations, and in the liver at autopsy. Panmyelophthisis marked the final stage.

RADIOLOGY

Pulmonary Changes in Dissem[illegible]d Lupus Erythematosus. J. M. Falomir. Gac. med. Mexico 89: 389-401 (May) 1959 (In Spanish) [Mexico, D. F.].

Five women, between the ages of 16 and 47 years, with disseminated lupus erythematosus, were observed in the Hospital de Enfermedades de la Nutrición of Mexico City. Three patients had the typical "butterfly" erythematous dermatosis and lupus cells in the peripheral blood. Two had neither. The patients had anemia, leukopenia, symptoms of an acute infection, and moderate disorders of respiration. The disease had lasted for several months or for several years. The patients remained hospitalized for a period which varied between 1 month and 10 months, up to occurrence of death. They were treated during the period of hospitalization with antibiotics and cortisone. Roentgenograms of the chest showed severe pulmonary lesions which were not suspected from the moderate clinical symptoms of the patients. Serial roentgenograms showed that the patients were in different stages of the pulmonary disease. There was a definite roentgenologic pattern which corresponded to the 3 progressive stages of the disease. The first stage was marked by bilateral interstitial pneumonia and pleurisy. Pneumonia was mainly localized in the lower lobes of the lung. The lesions changed from one region to the other of the lung for a certain period of time. Pleurisy changed from one to the other side of the thorax during the changes of the pulmonary lesions. The second stage was marked by stabilization of the pulmonary lesions and of the pleurisy. Mediastinal enlarged lymph nodes and occasional cardiomegaly appeared. The last stage was marked by final pneumonia and bronchopneumonia, increased size of the mediastinal lymph nodes, and cardiomegaly. The pulmonary changes found during an autopsy corresponded to those of final pneumonia and bronchopneumonia with hemorrhages of the vascular walls. The author concludes that roentgenograms of the chest of young women showing unstable interstitial pneumonia and pleurisy are specific of disseminated pulmonary lupus erythematosus if the patients had anemia, leukopenia, and symptoms of an acute infection, whether or not they had facial erythematous dermatosis. The pulmonary lesions and pleurisy which mark the first stage of pulmonary lupus erythematosus do not become stabilized under the effect of antibiotics or of cortisone.

X-Ray Diagnosis of Carcinoma of the Breast. D. M. Sklaroff, S. M. Berger and L. Moore. South. M. J. 52:1198-1205 (Oct.) 1959 [Birmingham, Ala.].

The authors made one or more roentgenologic studies of the breasts of 2,983 women during the 3 years from 1955 to 1958. They describe the characteristic roentgenologic aspects of 3 types of breast cancers: (1) the scirrhous, (2) the circumscribed, and (3) the intraductal growths. They discovered with the aid of roentgenoscopy among the nearly 3,000 women 79 mammary neoplasms which had not been suspected clinically. Sixteen of these were found on periodic x-ray screening in completely asymptomatic women. Over 68% of clinically unsuspected and asymptomatic neoplasms detected on x-ray study were less than 2 cm. in diameter, while the mean size of clinically diagnosable cancers was between 3 and 3.9 cm. Clinically evident neoplasms had metastases to regional lymph nodes in 66.4% of cases as opposed to an incidence of 30.4% metastases in the clinically unsuspected group.

The authors present the histories of 3 patients in whom the breast roentgenograms had shown neoplasms 5½, 6, and 15 months before operation. In 2 of these no mass was felt at operation, in spite of a characteristic x-ray appearance and evidence of growth during the lapse of time. None of these 3 patients had axillary metastases at operation. X-ray examination of the breast is urged for women in whom the clinical findings are not alarming and operation is not contemplated. Situations in which the clinician would hesitate to recommend operation while an x-ray examination would be of value are as follows: 1. The patient complains of a breast mass, but no mass is palpable to the examiner. 2. A patient has localized or unilateral breast pain, but no palpable mass. 3. A vague, soft, hardly definable thickening is palpated, and doubt exists on the significance of this finding. 4. Patients have multiple or bilateral breast masses, but one or more previous surgical interventions have shown only benign breast disease. 5. Patients in the cancer "age group" have a family history of breast cancer, and no abnormal clinical findings whatsoever.

PHYSIOLOGY

Morphologic Demonstration of Two Lymphocyte Systems in Man. E. G[illegible] [illegible], Wchnschr. 37:941-946 (Sept. 15) [illegible] [Berlin].

In earlier studies on the lymphatic organs of rats the author had discovered 2 lymphocytic systems, differing in both localization and structure. Studies by other investigators had led to essentially the same results in other rodents (rabbits), and some observations on human subjects suggested similar possibilities. The author's studies on humans are described in this report. Studies were made on tissues from young children who had died suddenly, because the formation of lymphocytes in young children is intense and not yet changed by inflammatory processes. Cytomorphologic studies were made on cut sections prepared from crushed specimens of the vermiform appendix. As in rats, 2 types of lymphocytes, differing in origin and in structure, could be distinguished. The first, a macronucleolar form, originates exclusively in the nodules of the lymph nodes. The second, a multinucleolar form, originates chiefly in the sinuses of spleen and of lymph nodes and in the basic lymphatic tissue of the lymph nodes, and, in contradistinction to the findings in rats, also in the dark nuclei of the peripheral zone of the lymph nodes. The 2 types of cells are most distinctly differentiable by phase-contrast microphotography in the crushed specimen, but also in the peripheral blood smear after treatment with a modified methylene blue stain.

Blood smears from 20 healthy persons, 15 adults and 5 children, were studied. It was found that about 72% of lymphocytes belong to the first type, that is, to those originating in the nodules of the lymph nodes, whereas the remaining 28% of lymphocytes are of sinus origin. In children of prepuberal age the ratio is 79:21% in favor of the lymphocytes of nodular origin. Each type of lymphocyte passes through its own phase of maturation.

Physiological Aspects of Human Fatigue. W. S. Frederik. A. M. A. Arch. Indust. Health 20:297-302 (Oct.) 1959 [Chicago].

The author performed preliminary studies by subjecting pilots to tests of fairly simple character. None of the methods and tests used provided any objective indication of the existence of fatigue, whereas on several occasions the pilots experienced a pronounced subjective fatigue. In a second series of laboratory experiments a group of persons was tested for several days during which no rest or sleep was taken whatsoever. During the entire experiment (3 × 24 hours) the ambient circumstances (i. e., temperature, illumination, intake of food, order in which tests were given) remained stable. The main senses, the nervous system including the cerebrum, the respiratory and circulating systems, and some glands of internal secretion were tested. Some of these tests showed deterioration at a fairly early moment, and others after 1, 2, or 3 days; still others did not show any deterioration of performance at all. Thus, the moment at which "fatigue" showed itself as a deterioration in performance was mainly dependent on the test itself. The person was "tired" at a certain moment only for that particular test.

This remarkable property led to a new series of experiments in which the author could prove that a person who showed "fatigue" for a specific job or task could perform other work without any difficulty. These findings prompted the introduction of the concept of "functional fatigue." Functional fatigue has been defined as being the state of a person in which the capability of performing a certain task has decreased below a permissible limit. By objective fatigue the author denotes deterioration in performance which actually can be measured. Subjective fatigue is simply the sensation of fatigue but does not imply a decrease in concentration and conciseness. What was really needed was a practical method of measuring or predicting the onset of objective functional fatigue, in which the function is not the operation of a gadget or the performing of an unrelated test but the flying of an airplane or the driving of a trailer truck.

Further investigations showed that the simultaneous performance of 2 tasks produces after a certain time a deterioration which is noticeable in each part of this combined task. The test person may be well able to perform at about the same time either of these tasks without any difficulty. The determination of the onset of functional objective fatigue of a complex task, such as flying an airplane, therefore, could be done by analyzing the results of an additional test which is performed by the pilot simultaneously with his performance. As an additional task, the measurements of choice reaction-times were selected, and a special device, the "performance indicator," has been developed, which presents graphically the choice reaction-time distribution with great accuracy. The performance indicator works fully automatically, and the onset of functional objective fatigue is indicated by a significant change in the shape of the reaction-time distribution.

The Mechanism of Inhibition of Gastric Acid Secretion by the Duodenum. T. W. Jones and H. N. Harkins. Gastroenterology 37:81-86 (July) 1959 [Baltimore].

In an attempt to clarify whether the fairly well-established inhibition of gastric secretion, in both volume and concentration, by the presence of acid in the duodenum is of nervous or hormonal origin, or a combination of both, the authors studied the isolated duodenum in a group of 4 dogs, 2 with Heidenhain pouches and 2 with Pavlov pouches. Various test substances, such as isotonic sodium chloride solution, 0.1 *N* hydrochloric acid, and 0.1 *N* sodium bicarbonate, were infused into the duodenum, and the effect of these substances on gastric acid secretion was noted. The results showed that under the conditions of this experimental study the duodenum can and does exert a hormonal inhibitory influence on free hydrochloric acid secretion from Heidenhain and Pavlov pouches. It also appears that under certain other circumstances the duodenum can exert a stimulatory influence on such gastric acid secretion. The mechanism of this stimulation may also be hormonal. These findings emphasize again the importance of the duodenum in the normal control of gastrointestinal physiology.

BOOK REVIEWS

Symposium on Basic Research, Sponsored by the National Academy of Sciences, the American Association for the Advancement of Science, and the Alfred P. Sloan Foundation, and Presented at the Caspary Auditorium of the Rockefeller Institute, May 14-16, 1959, New York City. Dael Wolfle, editor. Publication No. 56, of American Association for Advancement of Science. Cloth. $3; $2.50 prepaid to A. A. A. S. members. Pp. 308, with illustrations. American Association for Advancement of Science, 1515 Massachusetts Ave., N. W., Washington 5, D. C., 1959.

This report of a three-day conference presents a series of papers by outstanding leaders in science, government, education, and industry on problems general to all scientific work. In a discussion of the relationship of pure science to technology the need for cross-fertilization of ideas in research was emphasized. The question of governmental support was fully aired, and, in this connection, the speakers urged that the independence of teaching institutions be protected, that individual initiative be encouraged, and that even projects that have small chance to succeed be promoted so that new ideas and methods might be explored. During the discussion of the possible choice confronting the research scientist it was maintained that a scientist could live with an apparent paradox in doing what his interests impelled as well as what society expected of him, since there is no incompatibility between the effort of the individual person and that of the team. A strong plea was made for the kind of unification which would permit scientists to pursue their research without being engulfed in group effort.

The views of the universities and colleges were presented through addresses by the presidents of a small liberal arts college, a large state university, and a technological institute. All three speakers maintained that colleges must foster freedom of the individual and independence in research. It was pointed out that the government should assist in developing adequate financing programs which would permit teaching institutions to initiate projects for training and development of scientists on a long range basis and that emphasis should be shifted from applied to basic research. It was generally agreed that industry must recognize its role by expanding its effort in the field of basic research through improved relationship with teaching institutions and faculty consultants. It was pointed out that private philanthropies can play an important role by encouraging freedom of thought and effort and by encouraging the establishment of career investigatorships which would aid in returning the responsibility for progress to the universities and colleges. The highlight of the meeting was a speech by President Eisenhower on the first day of the conference.

The symposium attempted to discourage compartmentalization of research and emphasized the idea that any program should be an integral part of a larger program for support of creative scholarships in the broadest sense of the term. A major objective of basic research might be "the never-ending search for better understanding of man himself and of the total world, animate and inanimate, in which he lives."

Basic Bacteriology: Its Biological and Chemical Background. By Carl Lamanna, Ph.D., Scientific Director, Naval Biological Laboratory of School of Public Health, University of California at Berkeley, and M. Frank Mallette, Ph.D., Associate Professor of Agricultural and Biological Chemistry, Pennsylvania State University, University Park. Second edition. Cloth. $13.50. Pp. 853, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1959.

The first edition of this work was published in 1953 as a textbook of bacteriology at the advanced college or beginning graduate level. Little or no consideration was given to other microorganisms or to related subject matter such as bacterial toxins or immunology. This restricted approach has presumably filled a need, for the present edition continues it. The book is now somewhat longer and has been brought up to date in all respects.

The subject matter includes morphology, physical and chemical properties, growth and metabolism, and genetics of bacteria. Lysogeny is discussed in relation to bacteriophage-mediated transduction, but no other viruses are considered. The material is covered competently, and the representation of metabolic pathways is much better than that of the first edition. At the same time, the material is diluted by essentially extraneous considerations of certain aspects of chemistry in connection with staining and basic considerations of permeability. One would assume that the student should already have such information at hand. The space could have been devoted to a more well-rounded presentation. The excellent section on chemical disinfection is accompanied by the briefest possible consideration of the sulfonamides and antibiotics. That on enzymes and metabolism fails to cover the important area of bacterial toxins, including enzymatic and kinase activities associated with the virulence of the pathogenic bacteria, and the significant question of the formation of toxin by the anthrax bacillus in the tissues of the infected animal although not in culture.

The treatment as a whole avoids the subject of the pathogenic bacteria or any of their properties which may be associated with obligate parasitism

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

or disease. This attitude, deliberate or not, greatly detracts from the value of the book. The information omitted is the essence of the biological and chemical background, to quote the title, of the closely adapted parasites, whether or not they are pathogenic, and their chemical and biological makeup is reflected in their ecology, nutritive requirements, and similar basic properties. While this book can be a valuable reference source to those at an intermediate level of sophistication in the restricted areas covered, it has only limited value to those whose interests are not similarly confined.

The Golden Age of Quackery. By Stewart H. Holbrook. Cloth. $4.95. Pp. 302. The Macmillan Company, 60 Fifth Ave., New York 11; Brett-Macmillan, Ltd., 132 Water St., S., Galt, Ontario, Canada, 1959.

Mr. Stewart Holbrook, who has distinguished himself as a writer of bizarre episodes in American history, has now produced a most readable work in the area of nostrums and quackery. After confessing that his interest in this subject developed from his acquaintance with the late Mr. Samuel Hopkins Adams, he proceeds to attain an unusual degree of enthusiasm for the subject. Adams (whose exposures in *Collier's Magazine* at the turn of the century had a profound effect on the promotion of drugs), the A. M. A.'s late Dr. Arthur Cramp, and the iconoclast H. L. Mencken were in the forefront of the fight against quacks, nostrum makers, and cultists.

Mr. Holbrook recounts stories of the amazing success of fraudulent products, attractive but worthless gadgets and schemes, the early history of some old-timers in the nostrum field that are still found on druggists' shelves, alcoholic tonics, "cures" for all kinds of disease, and "doctors" whose ideas leaned toward the victimizing rather than the healing of hopeful patients. Physicians should enjoy reading this book, because it defines effectively a problem which, in all probability, will persist—that is, man's inclination to diagnose his own ailments. There is a recurring crop of entrepreneurs to urge him along—at their profit. What should particularly interest physicians, however, is the story of the part played by the American Medical Association in the constant fight against quackery through exposure of quacks and of the worthlessness or danger of their nostrums.

The Essentials of Roentgen Interpretation. By Lester W. Paul, M.D., Professor of Radiology and Chairman of Department of Radiology, University of Wisconsin Medical School, Madison, and John H. Juhl, M.D., Associate Professor of Radiology, University of Wisconsin Medical School. Cloth. $25. Pp. 839, with 1203 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1959.

In preparing this volume the authors' aim has been to organize and describe the basic concepts of roentgen interpretation and to bridge the gap between an elementary text and the multiple-volume reference work. This has been satisfactorily accomplished in a single volume covering the entire field of roentgenologic diagnosis in a clear and concise manner. When necessary, methods of roentgenologic examinations are described. Differential diagnosis of the more common diseases is emphasized. The preparation of the patient prior to examination is discussed, as well as care before and after certain investigations.

The content is considered under the following headings: osseous system; brain and spinal cord; abdomen and gastrointestinal tract; urinary and female genital tracts; chest; and face, mouth, and jaws. A short introduction concerning discovery and nature of roentgen rays, equipment, and definitions and an appendix dealing with radiation hazards in roentgenologic diagnosis enhance the value of the book. The logically organized and concisely written subject matter is illuminated with superb and carefully selected reproductions of roentgenograms.

The bibliography at the end of each chapter in some instances is somewhat scanty, but references have been carefully selected. The binding seems excellent, but the size of the book (7 by 11 in.) may not be conducive to durability. The authors and publishers are to be commended for providing the profession with this excellent textbook, which is recommended without reservation. It is probably the most comprehensive and best illustrated one-volume work available dealing with roentgenologic interpretations. It should be of definite value not only to the undergraduate student and resident but also to the practicing physician and surgeon who requires a ready reference book.

Symposium on Glaucoma. Editor: William B. Clark, M.D., F.A.C.S., Professor of Clinical Ophthalmology, Tulane University School of Medicine, New Orleans. Associate editor: Joe M. Carmichael, M.S.J. Transactions of New Orleans Academy of Ophthalmology, 1957. Cloth. $13.50. Pp. 314, with 99 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1959.

This volume reports the proceedings of the symposium on glaucoma held at the New Orleans Academy of Ophthalmology in 1957. The participants included Drs. Bernard Becker, W. Morton Grant, Joseph S. Haas, A. Edward Maumenee, Harold G. Scheie, Kenneth C. Swan, Georgiana Dvorak-Theobald, and Lorenz E. Zimmerman. The editor has done an excellent piece of work. The book is well written and pleasingly presented. All phases of glaucoma are discussed. Little new material is presented, but the contributors have summarized their views ably. One of the most interesting and valuable parts of the book is the question and answer section. The editor has retained an air of spontaneity which adds to the interest. If one small criticism might be voiced, it is that questions and answers pertaining to one subject or group of subjects might have been included with that subject rather than placed at the end of the book. This book is highly recommended to all ophthalmologists, but it is too technical to appeal to anyone not specializing in ophthalmology.

QUESTIONS AND ANSWERS

COMPLICATIONS OF CHEST TRAUMA

To the Editor:—*What is the relationship between trauma to the chest wall and pneumonia or pleural effusion? In one patient, no area of abrasion or contusion was apparent on the chest, and no ribs were fractured. Pneumonia with pleural effusion developed six days after the accident.*

Edwin P. Bickler, M.D., Milwaukee.

Answer.—Traumatic pleural effusion and pneumonia are rather uncommon conditions, and many physicians deny that ordinary trauma to the chest can precipitate pneumonia. Localized traumatic pleurisy is relatively common after a sharp blow to the chest, although there may be no external evidence of injury or rib fractures. It usually is localized directly under the point of impact. The pain usually disappears within one week and without complications. Occasionally effusion may develop, subsequent to such a localized pleural irritation, over a period of several weeks. These effusions generally are noninfectious but can be tuberculous if a tubercle on the pleura has been ruptured. When pneumonia occurs after a traumatic pleural effusion, it usually is due to a preexisting, unrecognized bacteremia or an infection in the smaller bronchi.

MANAGEMENT OF CATARACTS

To the Editor:—*Is there any medical method of preventing cataract formation? Six years ago an optometrist discovered that a cataract was starting in the lens of my right eye, and six or eight months later one was starting in the left. They have not as yet obscured my vision, but they are progressing to the center. I am taking 2.5 Gm. of potassium iodide per day in an attempt to check the growth. Would hot moist pads be helpful?*

Jane E. Dunaway, M.D., New Wilmington, Pa.

Answer.—There have been reports of various medicaments which are alleged to arrest the development of cataracts, but scientific investigations have failed to substantiate them. There is no evidence to support the administration of potassium iodide as treatment for cataracts. An optometrist should not evaluate the results of treatment, and the patient should consult an ophthalmologist. It is important that the lens be examined with a slit lamp biomicroscope by a physician familiar with ocular pathology, because there is the possibility of complications such as hypermaturity.

PHYSICIANS AND EYE EXAMINATIONS

To the Editor:—*Would you please distinguish among the following groups: oculists, optometrists, and ophthalmologists. For routine eye examinations in children, would one be more qualified than the others?*

Keith E. Vincent, M.D., Vallejo, Calif.

Answer.—The name oculist is synonymous with ophthalmologist—a physician (Doctor of Medicine) specially educated in all diseases and conditions of the whole visual system, i. e., the eyes, their adnexae, and the afferent and efferent visual pathways. He has the same responsibility to a patient as any physician, i. e., to make a diagnostic medical examination and prescribe whatever treatment is required (including glasses).

The word optometry was introduced by the ophthalmologist Landolt, in 1877, to describe the measurement of the refraction of the eye. The term was adopted about 1900 by the refracting opticians as a description of their occupation. The refracting opticians (who supplied glasses on the basis of tests they made, as distinguished from dispensing opticians who supply glasses on a physician's prescription) thereafter designated themselves optometrists. State laws defined the practice of optometry as the determination of the powers of vision and the application of glasses for the aid thereof. Some states have enlarged this definition to include (1) other methods of treatment, often having no scientific basis, such as exposing the eye to colored lights, and (2) some established medical procedures, such as psychotherapy, application of contact lenses, and orthoptics. No state authorizes the use of drugs or surgery nor does any require a medical training of persons desiring to practice optometry.

Although an optometrist may desire and feel that he is able to diagnose and treat patients for ocular conditions other than errors of refraction, he is not a physician, since he has not received a medical education. He is not qualified to make a medical diagnosis. Training of optometrists varies widely. Columbia, Illinois, and Rochester Universities have abandoned the teaching of optometry and no longer teach refraction outside the medical school. The Judicial Council of the A. M. A. stated in a report endorsed by its House of Delegates, December, 1955: "Its [optometry's] function is to determine mechanical defects of the eye and to correct them by the prescription of proper lenses." Optometrists are not "qualified . . . to do more than ascertain if mechanical defects exist and to correct them when necessary. In the absence of mechanical defect,

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

the optometrist should refrain from offering advice or treatment." (*J. A. M. A.* 159:927 [Oct. 29] 1955.)

If a child is to have an eye examination because of symptoms or as a preventive measure, the parents will want to know if an abnormal eye condition exists and they are entitled to advice concerning all treatment that may be required. Eye symptoms can be due to ocular disorder, metabolic disorder, brain tumor, and other conditions. Total evaluation of ocular findings requires medical training and competence. Children deserve a diagnostic examination by an ophthalmologist before glasses are prescribed and fitted.

BIFOCALS IN CHILDREN

To the Editor:—*The answer to the question in* The Journal, *July 25, page 1618, seems to have missed the intention of the inquirer. The bifocal lenses to which the inquirer wished to refer were those being prescribed for teenagers and younger children with myopia. Had this specific condition been indicated in the question, the consultant would have made an entirely different answer. There is no scientific evidence that bifocal lenses, now being prescribed by the thousands by nonmedical refractionists, have any effect in decreasing the myopia which normally occurs with growth and age. In fact, most youngsters with such bifocal lenses usually use only the upper part of their glasses for all visual activity and get no benefit from the added correction for so-called aid in accommodation. In the young myopic patient, axial myopia progression may cease spontaneously and at any time, regardless of any appliances or therapy being used at that time. There is good reason for prescribing a full-distance correction for these patients. It causes them to read with the print at a distance of 15 or 16 in., avoiding the mechanical pull of the internal rectus muscles on the sclera and elongation of the eye ball secondary to the excessive attempt at convergence.*

Ralph O. Rychener, M.D.
1720 Exchange Bldg.
Memphis 3, Tenn.

To the Editor:—The Journal, *July 25, page 1618, contained a letter and answer concerning the use of bifocal lenses for children and teenagers. The question was well stated and the answer excellent. Some optometrists will prescribe bifocal glasses for youngsters who have no disability other than myopia. These optometrists apparently reason that the use of the normal accommodative mechanism will increase myopia; however, when they substitute accommodation by means of a bifocal lens, the child subsequently loses the ability to exert full accommodation. Luckily, this induced weakness for near vision can be corrected by prescribing single-vision glasses and instructing the child to do his close eye work with the same glasses that he uses for distance. The prescription of bifocal glasses for children with myopia is to be avoided and condemned.*

Arthur E. Halpern, M.D.
70 N. E. Second St.
Miami 32, Fla.

To the Editor:—*In* The Journal, *July 25, page 1618, the answer as to the use of bifocal lenses in children was complete, but an error appeared in the second part. The error should be corrected, since bifocal lenses are worn by children more often for motor imbalance than for paralysis of the accommodative mechanism or for subnormal vision. The answer stated that the bifocal lens was useful in esotropia that is greater for distant than for near vision. It should be the other way around. Bifocal lenses are useful in esotropia that is greater for near than for distant vision. Looking at a distant object through a bifocal lens will blur the vision. Looking through the bifocal lens at near objects will help decrease the accommodative effort necessary both to see at close range and to achieve convergence.*

Capt. Thomas J. Tredici
U. S. A. F. Hospital
Clark Air Force Base
APO 74
San Francisco

DIGITALIS AND PLACENTAL BARRIER

To the Editor:—*In* The Journal, *Aug. 29, page 2265, there is an answer to the question "Does digitalis pass the placental barrier? If so, is it harmful to the fetal heart?" Drs. Okita and Davis and I reported on the use of radioactive digitoxin in this connection* (Circulation Res. 4:376 *[July] 1956). The results of these studies do not confirm the opinion expressed in the answer in* The Journal.

Ernst J. Plotz, M.D.
The Chicago Lying-In Hospital
5841 Maryland Avenue
Chicago 37.

The above comment was referred to the consultant who answered the original question and his reply follows.—Ed.

To the Editor:—*At the time I prepared the answer to the question in point I was not aware of the excellent article by Okita, Plotz, and Davis. They have shown conclusively that digitoxin does pass the placenta and reaches the fetus. Their conclusion is that the low percentage of the drug found in the fetus may be considered to be nontoxic to the unborn child.*

WASHINGTON NEWS

Drug Hearings . .
Kennedy Bill . .
Chemical Additives Control . .
Influenza Forecast . .

PROBERS QUESTION DRUG ADVERTISING, PRICES

The Senate antitrust subcommittee wound up a second round of hearings on drug manufacturers with subcommittee chairman Estes Kefauver (D., Tenn.) challenging the accuracy of some advertisements and accusing the industry of making "exorbitant" profits.

The hearings "show definitely that something ought to be done" about legislation restricting advertising by drug companies, said the Tennessee Democrat.

Officials of four major producers of tranquilizing drugs—CIBA, American Home Products, Carter Products, and Smith Kline & French (SKF)—disputed Kefauver's statements. They noted that even if they eliminated profits altogether the price of their products to consumers would drop only slightly. As for advertising, they denied any misleading statements and said that the advertisements were not intended to convey all the technical information about drugs or to serve as the sole basis for a physician's prescription.

As the hearings were taking place on Capitol Hill, The Justice Department announced it had filed an antitrust suit in New York against Carter Products and American Home Products. The suit charged that the two companies had agreed to exclude all others from the manufacture and sale of tranquilizing preparations made with meprobamate, agreed to fix prices of meprobamate tranquilizers, and agreed on who will make and sell other drugs in which meprobamate is used.

The leading Republican member of the subcommittee, Sen. Everett M. Dirksen (R., Ill.), charged that the subcommittee statistics on profits were misleading. He said the investigators failed to consider necessary spending on research, promotion, and other overhead items as well as the risk involved in the drug industry.

Dirksen, the Senate GOP leader, said the previous hearings on steroid drugs in December appeared to be "terribly unfair and completely inequitable" by "distorting" the difference between raw materials and the finished product. On the same basis, Dirksen said, a loaf of bread cost only 2 or 3 cents.

Kefauver repeatedly asserted that the investigation was not intended "in any way to be critical" of the present method of private medical practice. He later declared that the American Medical Association and physicians that the group had heard from were very much concerned about the welfare of their patients. He referred to the AMA's Council on Drugs as "that great association of this country."

SKF President Walter A. Munns, the first drug industry witness, stressed the value of tranquilizers for treating mental patients and discussed the research necessary for his company to place the tranquilizer chlorpromazine on the market in this country.

Munns said that if the company were to operate at no profit at all, the price of tranquilizers to private persons would drop only 2 or 3 cents a day. The problem of patients returning to mental hospitals because they cannot afford to pay for tranquilizers is a serious one that SKF has been grappling with for some time, he said. Some people cannot afford drugs they need, but the solution is not in reducing the cost by a few cents, he said; rather, some satisfactory way of supplying the drugs through government or private channels should be found.

The research and risk involved in producing prescription drugs demands relatively high profit margins, said Munns, especially in view of the fact that a competitor overnight could come up with a product that could ruin the market for a drug.

Henry H. Hoyt, president of Carter Products, testified that the company earns a profit of about 1 cent a tablet on Miltown and that the price is reasonable. He agreed that Carter's profits had been high in the past four years but said they should be compared to the 13 preceding years in which the company had had a hard time making ends meet.

He urged the subcommittee not to recommend any changes in the drug patent field, declaring that patent rights are necessary for the survival of small drug companies.

The next witness, Dr. Frank M. Berger, president of Carter's Wallace Laboratories Division, defended advertising of Miltown in medical journals and said he was sure that general practitioners do not prescribe drugs merely on the basis of magazine advertisements. He noted that Wallace Laboratories each year sends to physicians a booklet with up-to-date technical information on Miltown. The magazine advertisements, he said, are intended to remind busy physicians of the existence of the drug and its general attributes and not to contain a full presentation.

Noting that there had been some criticism of advertisements for tranquilizers for not mentioning side-effects or possible addictive qualities, Dr. Berger said any potent drug may have toxic effects, and, "We assume physicians consider the relevant factors before prescribing any drug."

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Lown, B., and Levine, S. A.: Current Concepts in Digitalis Therapy, Boston, Little, Brown & Company, 1954, p. 23, par. 2.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

Mike Gorman, director of the National Committee Against Mental Illness, said the drug industry was "directly" responsible for the return of patients to mental hospitals, placed "nauseating" ads in medical journals, and inflated research figures. He recommended tight federal supervision of the industry.

Senator Dirksen said he thought Gorman was exaggerated in his critical attack and had "gone a little far afield."

Meanwhile, a spokesman for the drug industry declared that publicity resulting from the Senate inquiry is "creating a distorted image" and is "seriously disturbing public confidence in the medical care provided in the United States."

"We welcome scrutiny," Dr. Austin Smith, president of the Pharmaceutical Manufacturers Association, said, "but it is another matter when investigations resulting in scare headlines unfold. To seek the facts is laudable. But to prejudge or to err by depending in part on meaningless or questionable figures which may project a confusing, even distorted, picture of a subject that under the best circumstances may be too closely related to easily disturbed emotions is unfortunate."

SENATOR KENNEDY INTRODUCES FORAND-TYPE BILL

Sen. John F. Kennedy (D., Mass.), a leading contender for the Democratic presidential nomination, introduced a sweeping bill that would provide health care financed by the Federal government for all social security beneficiaries.

The Massachusetts senator's bill is much broader than the measure sponsored in the House of Representatives by Rep. Aime J. Forand (D., R. I.).

Senator Kennedy declared in a Senate speech that "the time is long past when there was any question about the need for this legislation."

Kennedy disputed contentions by the administration, the health insurance industry, the American Medical Association, and other groups that the problem is well on the way to being solved through private, voluntary means. Opponents to the legislation warn that it would be the first step toward government control of most aspects of private medical and hospital practice.

FLEMMING SEEKS BROADER AUTHORITY OVER ADDITIVES AND COLORINGS

Arthur S. Flemming, Secretary of Health, Education, and Welfare, went before Congress to defend his policies in cracking down on possibly harmful chemical additives and pesticides and urged wider authority to protect consumers against such substances.

Testifying before the House Commerce Committee, the secretary, who has been under fire for HEW actions involving cranberries, milk, and chickens, said that the government had a responsibility to protect the public against unnecessary risks such as cancer through the food supply.

"No one knows how much or how little of a substance will induce cancer when added to the diet of man," he testified.

Flemming specifically asked the committee to include in a pending bill on color additives a clause prohibiting any coloring that is found to induce cancer in test animals. The over-all bill would require food processors to submit proof of the safety of colorings to the government, allow the government to set tolerances on colorings that in large quantities could cause harm other than cancer, and bring all colorings under federal regulation. At present, only coal-tar dyes are regulated.

The Senate approved the bill last year but did not include the flat ban on colorings that cause cancer in test animals.

Flemming also recommended that the Food and Drug Administration be given power to revoke prior approvals for food additives without the necessity of going to court. Although the agency may deny new applications for additives considered unsafe and require applicants to offer prior proof of safety, previously cleared substances cannot be barred automatically even if later tests find them to be harmful.

Another proposal by Flemming would modify the law governing cancer-inducing substances that are fed to animals but leave no residue in the food consumed by man. FDA should be allowed to grant clearances in such cases, he said.

REPORT ON INFLUENZA

The U. S. Public Health Service predicted this year's influenza epidemic will be less severe than the one in 1957.

Laboratory tests in seven states and the District of Columbia have identified the disease as the A-2 or Asian strain of influenza. Although no estimates were made of the number of persons afflicted, more than 500,000 cases were reported in the Los Angeles area alone.

The PHS forecasts outbreaks for the next several weeks in additional areas of the United States, with many probably starting in concentrated populations such as schools and factories.

"For the majority of individuals, the disease will be quite uncomfortable with fever and generalized aching, but with improvement within a week," said PHS. "For a small proportion of persons, the symptoms may become more severe and not improve rapidly. For these individuals it is especially important that a physician be consulted to be certain that no complications develop."

PHS Surgeon General Leroy S. Burney said that in general this year's outbreaks have not been as severe as the 1957 epidemic. However, in Texas and California the clinical impression of practicing physicians was that the disease was more severe than in 1957 and that the incidence of pneumonia was higher.

States reporting isolation of the Asian strain were California, Hawaii, Iowa, Michigan, Pennsylvania, Texas, Washington, and the District of Columbia. In addition, reports of influenza-like disease outbreaks were received from Kentucky, Mississippi, Nevada, Ohio, Tennessee, Utah, and West Virginia.

Dr. Burney repeated his advice that vaccination against influenza is especially desirable for persons in whom the disease would be an added health risk, such as persons with heart or lung disease, pregnant women, and persons over 55 years of age with any form of chronic disease. He pointed out that it takes three weeks after vaccination to develop protection against the disease.

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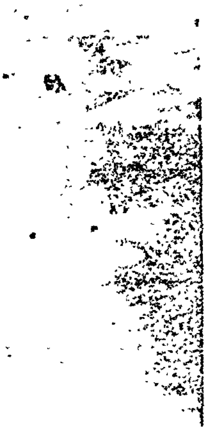

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 28-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 27-Dec. 1.
1962 Annual Meeting, Chicago, June 11-15.
1962 Clinical Meeting, Los Angeles, Nov. 25-30.

AMERICAN

1960

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 11-13. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, North Carolina Chapter, Hotel Barringer, Charlotte, N. C., Feb. 26-27. For information write Dr. Alexander Webb Jr., 201 Bryan Bldg., Cameron Village, Raleigh, N. C.

American College of Surgeons, *Sectional Meeting for Surgeons and* Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

American Academy of General Practice, Philadelphia, Mar. 18-24. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Mo., Executive Director.

American Association for the History of Medicine, Inc., Charleston, S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Institution, Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadmoor, Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Portland Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, New Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. of Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. 30. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Treasurer.

American Laryngological Association, Deauville Hotel, Miami Beach, Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Technology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Society, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Fla., Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneapolis 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, Montreal, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N. Y., Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Rico, Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory University, Atlanta 22, Ga., Secretary.

Association of Clinical Scientists, DeWitt Clinton Hotel, Albany, N. Y., March 3-5. Dr. Robert P. MacFate, 54 W. Hubbard St., Chicago 10, Secretary.

Intermountain Pediatric Society, Stardust Hotel, Las Vegas, Nev., Mar. 28-29. Dr. Joseph R. Newton, 2000 S. 9th East, Salt Lake City, Utah, Publicity Chairman.

Missouri State Medical Association, Sheraton-Jefferson Hotel, St. Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Louis 3, Executive Secretary.

National Health Council, National Health Forum, Miami, Fla., Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, Executive Director.

National Multiple Sclerosis Society, New York City, Mar. 8. Mr. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. 30-Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore 1, Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, New Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., New Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, Mar. 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Executive Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev., Mar. 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma City, Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Semmes Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jackson St., Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla., Apr. 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Executive Secretary.

American Association of Anatomists, Statler-Hilton, New York City, Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Medicine, Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, Chicago, Apr. 11-15. Dr. Calderon Howe, Columbia Univ. College of Physicians and Surgeons, New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, Hotel Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman, Dept. of Pathology, L. S. U. School of Medicine, New Orleans, La., Secretary.

American Association of Railway Surgeons, Drake Hotel, Chicago, Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Executive Secretary.

American College of Obstetricians and Gynecologists, Netherland Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardson, 79 W. Monroe St., Chicago 3, Executive Secretary.

American College of Physicians, Mark Hopkins & Fairmont, San Francisco, Apr. 4-9. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

American College of Surgeons, Sectional Meeting, Hotel Leamington, Minneapolis, Apr. 11-13. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Kahler Hotel, Rochester, Minn., Apr. 14. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, West Virginia Chapter, The Greenbrier, White Sulphur Springs, W. Va., Apr. 1-2. Dr. Ray E. Burger, Grace Hospital, Welch, W. Va., Vice-President.

American Dermatological Association, Inc., Boca Raton Hotel, Boca Raton, Fla., Apr. 8-12. Dr. Wiley M. Sams, 308 Ingraham Bldg., Miami 32, Fla., Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. Daggs, D.Sc., 9650 Wisconsin Ave., Washington 14, D. C., Executive Secretary.

American Proctologic Society, Shamrock Hilton Hotel, Houston, Texas, Apr. 25-27. Dr. Norman D. Nigro, 10 Peterboro, Detroit 1, Secretary.

American Public Health Association, Southern Branch, Memphis, Tenn., Apr. 13-15. Dr. L. M. Graves, Shelby County Health Department, Memphis, Tenn., Chairman, Local Arrangements Committee.

American Society of Biological Chemists, Inc., Chicago, Apr. 11-16. Dr. Frank W. Putnam, Dept. of Biochemistry, Univ. of Florida, Gainesville, Secretary.

American Society for Experimental Pathology, Pick Congress Hotel, Chicago, Apr. 11-15. Dr. J. F. A. McManus, Univ. of Alabama Med. Center, Birmingham, Ala., Executive Secretary.

American Society of Facial Plastic Surgery, Hotel Elysee, New York City, Apr. 6. Dr. Samuel M. Bloom, 123 E. 83d St., New York 28, Secretary.

American Society of Internal Medicine, Sheraton-Palace Hotel, San Francisco, Apr. 1-3. Mr. Robert L. Richards, 350 Post St., San Francisco 8, Executive Director.

American Society for Pharmacology and Experimental Therapeutics, Inc., Chicago, Apr. Dr. Karl H. Beyer Jr., Merck Sharp and Dohme Research Labs., West Point, Pa., Secretary.

American Society for the Study of Sterility, Sheraton-Gibson Hotel, Cincinnati, Apr. 1-3. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham 5, Ala., Executive Secretary.

(Continued on page 38)

THE JOURNAL

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FEBRUARY 6, 1960

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CONTACT ULCER OF THE LARYNX

Paul H. Holinger, M.D.
and
Kenneth C. Johnston, M.D., Chicago

The etiology, pathology, and treatment of contact ulcer of the larynx were studied in 92 patients whose ages ranged from 28 to 72 years. There was a significant preponderance of males over females (84 to 8). The most important etiological factor was the vocal strain of shouting against noise or talking under other adverse conditions. The lesions appeared as ulcers on those cartilaginous parts of the vocal cords that touch during phonation. Granulomas developed in the chronic cases, and some became extremely large. The symptoms included hoarseness and pain. Therapy began with voice rest and elimination of oral infection; these combined with vocal reeducation sometimes sufficed to bring about improvement. Surgical removal of the granuloma under direct laryngoscopy was done in 42 of the 92 patients. No cautery, either chemical or electrical, should be used.

CONTACT ulcer of the larynx is a unilateral or bilateral superficial ulceration of approximating surfaces of the arytenoid cartilages. It may develop along the medial surfaces of these cartilages at any point where there is contact during phonation. The lesion was first described as a distinct clinical entity by Chevalier Jackson[1] in 1928, and his observations at that time form the basis for definition and understanding of the condition. This review was initiated by discrepancies of concept of the lesion between laryngologists and speech pathologists.

Presentation of Case Material

This study is based on a series of 92 patients with contact ulcer of the larynx seen during the past 10 years. Conclusions regarding etiology, pathology, and treatment are obtained from an analysis of these cases.

Etiology.—The patients ranged in age from 28 to 72 years. Only two patients were less than 30 years of age, 15 were between 30 and 39, 32 between 40 and 49, 33 between 50 and 59, 8 between 60 and 69, and 2 more than 70. Most significant is the fact that, of the 92 patients, 84 were males and only 8 were females. This great preponderance of males is in agreement with that reported by the Jacksons.[2] Six of the eight females were between 41 and 51 years of age, the other two being 32 years of age; most were store clerks or had managerial positions, and one was a missionary. The occupations of the male patients constituting this series

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From the Department of Otolaryngology, University of Illinois College of Medicine, and the Presbyterian-St. Luke's Hospital.

Read before the Section on Laryngology, Otology, and Rhinology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

are recognized as being associated with vocal stress and strain.[3] There were 21 salesmen or brokers, 11 preachers or teachers, 10 physicians or dentists, and 9 managers of businesses; 6 were lawyers and 12 were factory or railroad workers whose jobs required shouting or talking over a loud noise. Other occupations such as bartender, traffic officer, "stock expediter," and union arbitrator seem significant in a review of etiology.

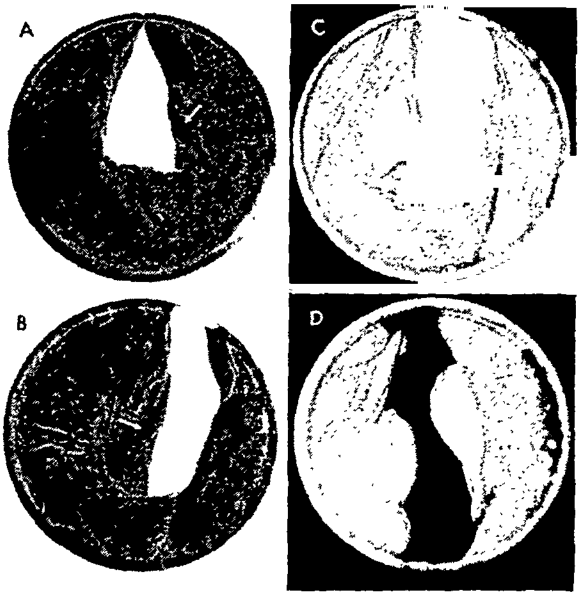

Fig. 1.—*A*, early, superficial contact ulcer of right arytenoid cartilage. *B*, superficial contact ulcer of tip of vocal of left arytenoid cartilage. Prominence of vascular pattern is evidence of severity of acute inflammatory process. *C*, granuloma and exudate on left arytenoid cartilage illustrating most frequently seen appearance of contact ulcer granuloma. *D*, bilateral contact ulcer granulomas with white, necrotic centers surrounded by pads of granulation tissue.

Excessive smoking was by no means a constant factor in patients in this series. Twenty-four of the 92 smoked one or more packages of cigarettes per day, with 6 of the 24 smoking between two and three packages per day. A number of patients had stopped smoking shortly before their first examination because of the persistence of throat symptoms due to the contact ulcer. However, 23 of the patients had not smoked at all, and 22 smoked less than one-half package per day. Nevertheless, in those patients who smoked, improvement in symptoms and in the gross appearance of the lesion was noted when they abstained from smoking, and there was generally a recurrence in symptoms and an exacerbation of the lesion if they started smoking again.

Twenty-six patients attributed the onset of symptoms to an acute upper respiratory infection, and in one patient a granuloma appeared on the opposite arytenoid cartilage immediately after an acute respiratory infection. Three men definitely related the onset of symptoms to yelling at bowling matches and four to singing and talking loudly at a boisterous party.

Allergy seemed to be a factor in several patients, as pain and discomfort were increased after eating certain foods or exposure to dusts. One patient stated that his symptoms always increased after eating chocolate. A farmer invariably noted an increase in pain and discomfort in the region of the thyroid cartilage after entering or working in a corn crib and another when working in a chicken yard or hen house.

Symptomatology.—Symptoms varied widely in degree. Severest symptoms were hoarseness and extreme throat pain radiating to one or both ears on talking. Such expressions as "something wrong with my throat," a "constriction or squeezing in the throat," and a "constant tendency or desire to clear the throat" were common in obtaining the history of the condition. Generally pain, discomfort, huskiness, and persistent sore throat constituted the majority of the complaints.[4] Excessive or loud talking, yelling, or, significantly, long-distance telephoning or dictating on a machine increased the severity of symptoms.

Pathology.—A contact ulcer originates on approximating cartilaginous surfaces of the arytenoid cartilages as a superficial, soft, shallow ulcer (fig. 1*A*). As the process continues, an increased vascularity is evidence of the inflammation characteristic of this clinical entity (fig. 1*B*). A granuloma may develop (fig. 1*C*) which is covered with white exudate to give the most typical appearance of a contact ulcer. Often the white mass is surrounded by a fine, bright red inflammatory zone, and in some cases the necrotic ulcer becomes surrounded by a large pad of granulation tissue (fig. 1*D*). In more chronic, long-standing lesions, the granuloma becomes or-

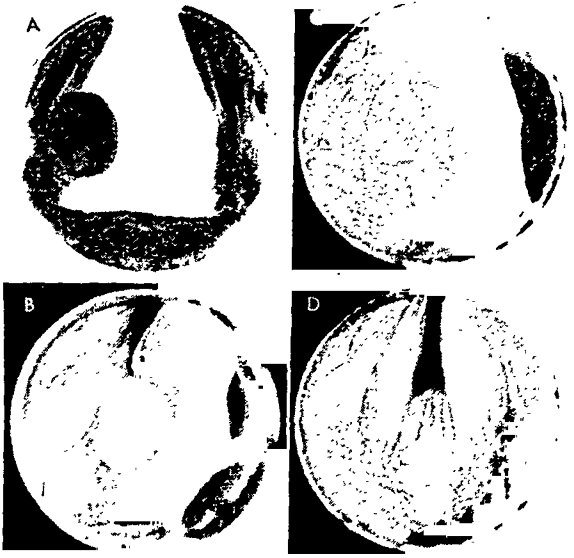

Fig. 2.—Direct laryngoscopic photographs of chronic contact ulcer granulomas. *A*, granuloma at level of superior surface of cord. *B*, granuloma above level of superior surface of cord. *C*, unusually large granuloma (inspiration). *D*, same patient, phonation.

ganized, smooth, and discrete (fig. 2*A* and *B*). Occasionally, it becomes extremely large (fig. 2*C*), sliding under the opposite cord during phonation or fitting directly into a deep crater on the opposite arytenoid cartilage (fig. 2*D*). In 26 of the 92 cases reviewed the ulcer or granuloma was on the right, in 35 it was on the left, and in 31 the lesion was bilateral. The difference between the gross appearance of these lesions and the postintratracheal intubation granuloma may be seen by comparing the photographs in figures 1 and 2 with the postanesthesia granuloma shown in figure 3.

Histologically, contact ulcers of the larynx consist of mucosal ulcers covered with tissue debris, inflammatory exudate, and granulation tissues in varying degree (fig. 4). In some sections, the interrupted epithelial margins are seen, with fibrinous exudate and the remaining surface epithelium showing swelling of the cells indicative of degenerative changes. As granulation tissues develop, these are found to contain leukocytic exudates and to consist of many capillaries and vascular channels. In essence, the lesion is a granulation tissue reaction to chronic irritation and inflammation.

Anatomically, most of the arytenoid cartilage is made up of hyaline cartilage; significantly, however, the vocal process and often the apex is composed of elastic cartilage. Cartilaginous contact occurs between the two arytenoid cartilages during phonation, swallowing, laryngeal spasm associated with coughing, sneezing, or the "glottal attack" in phonation, with only a thin mucosa covering the contacting surfaces. Forceful cartilaginous approximation takes place not only on the tip of the vocal process where the ulcer and granuloma are usually seen but may involve the entire medial surfaces of the arytenoid cartilages from the phonating edges upward toward the apex. Of particular importance is the colliculus of the arytenoid cartilages, consisting of a small nodule below the apex on the surface, looking medial and forward of each cartilage. These nodular contacting surfaces may indent the anteromedial aspect of the opposite side on phonation. In nine of the patients in this series, this point was the site of the ulcer, the remaining clinical and histological characteristics of the lesion being consistent with the lesions arising on the tip of the vocal process.

It is apparent that the ulceration which typifies a contact ulcer is produced by what Jackson [2] has designated as "the trauma of the hammer and the anvil." Explosive speech patterns consisting of a glottal plosive attack intensify the normal approximation of the arytenoid cartilages. A stress pattern is responsible for additional sphincteric contraction of the larynx in the tense type of person usually found to be afflicted with the condition.[4a]

With the development of the ulcer, granulation tissues arise as a reaction to the chronic irritation and inflammation. Infection and continued irritation and trauma are then responsible for the persistence of the lesion.

The clinical and pathological similarity between contact ulcer granulomas and the postintratracheal anesthesia granulomas (fig. 3) has been recognized.[5] The latter type of lesion has not been included in the statistical analysis of the series herein presented because of the common etiological factor in the postanesthesia granuloma. Furthermore, in the postanesthesia granulomas, the site of origin does not appear to be in the elastic cartilaginous vocal process tip or superior apex of the arytenoid cartilage but more posteriorly and inferiorly in the hyaline cartilaginous body of the cartilage. However, the basic histological pathology of the two lesions is identical, and factors responsible for their chronicity are likewise identical.

Treatment.—In a previous communication,[4b] the role of vocal reeducation was stressed as a therapeutic aid in the management of contact ulcer of the larynx. The present review of cases confirms the findings of the smaller series, namely, that vocal abuse is an important etiological factor in the production of the ulcer and is a perpetuating factor as well. Surgical removal of the granulomatous mass was necessary in some cases, but it was shown that this is only partially effective if voice correction and reeducation procedures are not used. Yet, the failure to obtain improvement consistently in spite of accurate removal of the inflammatory granuloma has led to a reanalysis of anatomic and pathological findings in an effort to improve the therapeutic regimen. Based on these studies, a rational course of therapy has been developed.

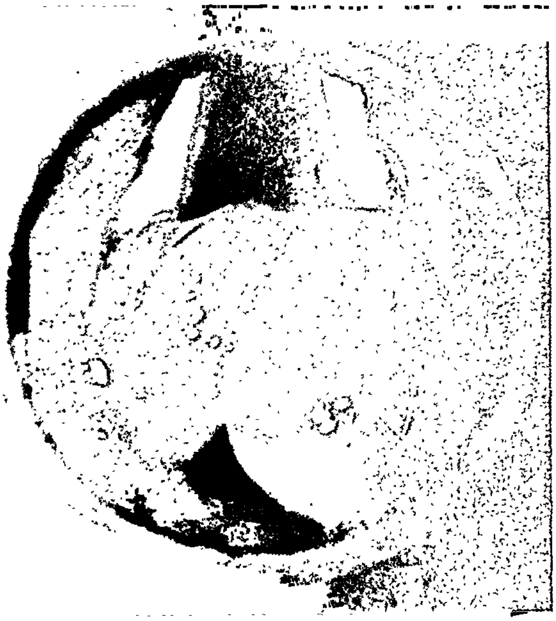

Fig. 3.—Postintratracheal anesthesia granulomas. Broader base extending along whole body of arytenoid cartilage differentiates this lesion from those associated with vocal trauma.

All patients are advised that a period of silence is desirable and effective in relieving symptoms. The need for loud talking must be removed. Improvement is usually seen in the appearance of the lesion if this is strictly adhered to. In acute ulcers, one to three months of silence may be necessary, the period of time determined by the appearance of the lesion and the severity of symptoms. Hot packs to the neck, antibiotics, and the removal of the patient from the irritation of smoke or fumes in industry are essential for relief of pain and discomfort in the acute stage. Vocal reeducation is advised and is instituted immediately in patients with chronic ulcers. In these patients, if the granuloma is not too well established and organized, improvement may be expected which will obviate a direct surgical removal of the excess tissue. However, if the granuloma is discrete, it is removed under direct laryngoscopy by surgical excision with a sharp cup forceps.

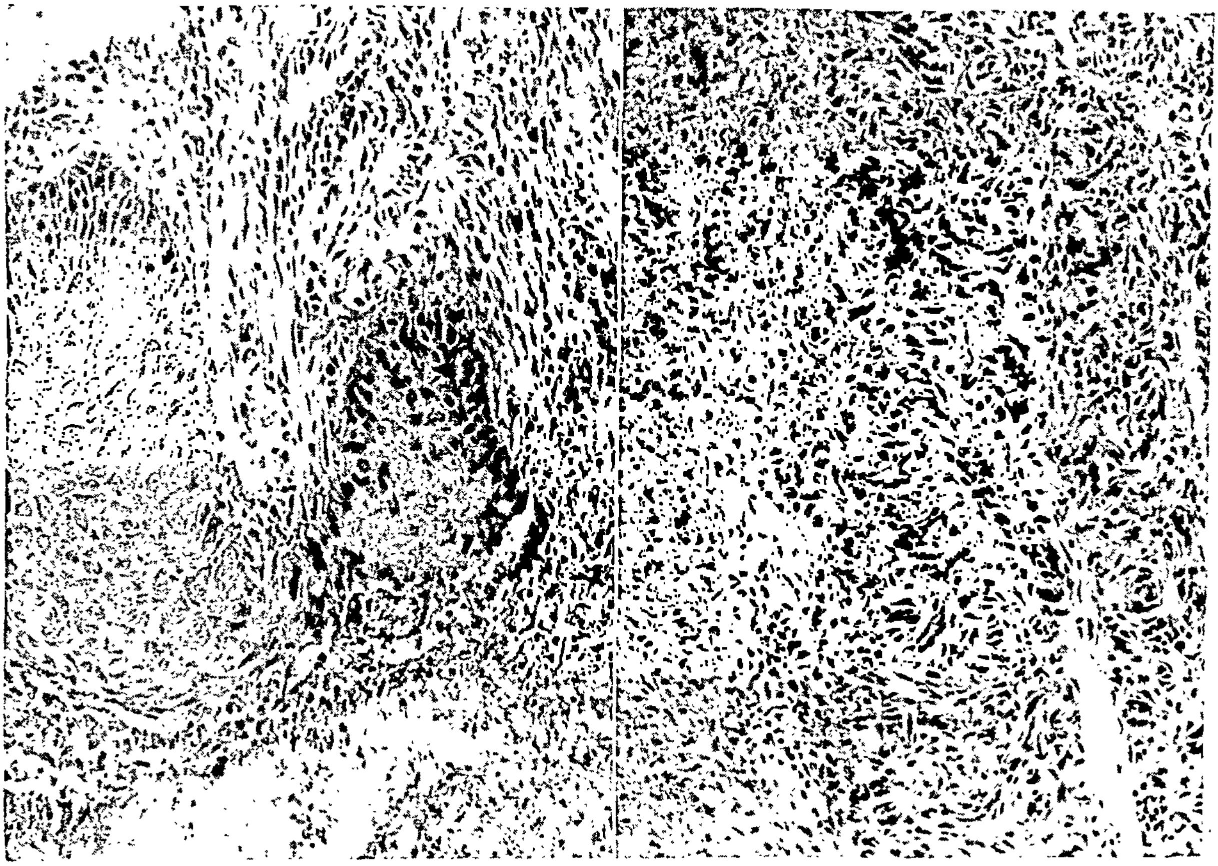

Fig. 4.—*Left*, histological appearance of contact ulcer and granuloma. Necrotic tissue debris and inflammatory exudates constituting surface of ulcer are seen with swollen epithelial cells in lower third of section, covered by granulation tissues. *Right*, granulation tissues on right with leukocytic exudates and many capillaries and vascular channels.

Direct laryngoscopy and surgical removal of the granuloma was done in 42 of the 92 patients. More than one procedure was necessary in 14. In view of the character of the lesion, no cautery, either chemical or electric, was used, since its use would only tend to increase irritation. This point has always been stressed by Jackson and Jackson, who indicate that the severest edema and inflammation noted in patients with contact ulcers were those seen after the use of cautery. The elimination of oral infection is essential.[6] In addition, the change of the pH of oral mucus is effective in reducing some of the factors of chronicity.

In four patients with persistent, painful ulcers, x-ray therapy was directed over the lateral aspects of the larynx, toward the arytenoid cartilages. The dosage consisted of two treatments of 75 to 100 r each. These dosages have, in the past, been used in inflammatory processes elsewhere in the body. This therapy was effective in three of the four cases. It should be strongly emphasized that higher dosages or a repetition of the treatments of this character should be strictly avoided for fear of causing a severe exacerbation of symptoms.

Summary

Contact ulcer of the larynx is a term designating ulceration of approximating surfaces of the arytenoid cartilages. It is usually produced by faulty, traumatic techniques of voice production. It affects those whose occupations are associated with constant voice use under pressure—pressures of selling (salesmen and brokers), public speaking (preachers, missionaries, lecturers), arguing (lawyers), and pressures of talking and shouting over loud noises (in heavy industry and railroading). The ulcer begins as a superficial erosion, usu-

ally on the vocal process of the arytenoid cartilage, but it may originate on the ascending approximating surfaces.

Chronic irritation and infection characterize the lesion histologically with necrosis, inflammatory exudates, and finally granulation tissue formation. Factors responsible for its chronicity are continued vocal trauma, oral sepsis, and local irritation and infection.

Therapy begins with voice rest and elimination of sources of oral infection. Subsequently, voice reeducation plays a prominent role. Surgical removal of the granuloma in the more chronic lesions is accomplished under direct laryngoscopy with sharp cup forceps, and in some cases this surgical attack must be repeated. Cautery is to be avoided. X-ray therapy (75 to 100 r) administered twice to the arytenoid area was of value in three of four patients with persistent pain and discomfort. A repetition of this therapy or an increase in the dosage must not be considered, since it would result in an exacerbation of the lesion.

Contact ulcer of the larynx is a serious occupational handicap. Teamwork between laryngologist and speech pathologist is essential in its management.

700 N. Michigan Ave. (11) (Dr. Holinger).

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2. Jackson, C., and Jackson, C. L.: Contact Ulcer of Larynx, Arch. Otolaryng. **22**:1-15 (July) 1935.

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4. (*a*) Peacher, G.: Contact Ulcer of Larynx: I. History, Speech Disorders **12**:67-76 (March) 1947. (*b*) Peacher, G., and Holinger, P.: Contact Ulcer of Larynx: Role of Vocal Reeducation, Arch. Otolaryng. **46**:617-623 (Nov.) 1947.

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6. Jackson, C. L.: Etiology and Treatment of Contact Ulcer of Larynx, Laryngoscope **43**:718-721 (Sept.) 1933.

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DIFFERENTIAL DIAGNOSIS OF CARCINOMA OF THE SIGMOID AND DIVERTICULITIS

EVALUATION OF AIDS

Joseph L. Ponka, M.D., Brock E. Brush, M.D.
and
J. DeWitt Fox, M.D., Detroit

In order to establish criteria for the differential diagnosis between diverticulitis and carcinoma of the sigmoid colon, a study was made comparing 100 patients with proved carcinoma of the sigmoid and 100 patients with every reasonable finding supporting the diagnosis of diverticulitis. The two conditions had many signs and symptoms in common, but certain generalizations were possible. Change of bowel habits, evidence of intestinal bleeding, anemia, and weight loss were more frequent in patients with tumors; pain, fever, and leukocytosis were more frequent in patients with diverticulitis. Roentgenographic study of the sigmoid colon gave the presumptive diagnosis of tumor in 84 patients and of diverticulitis in 29. Sigmoidoscopic examination and biopsy specimens were used as a basis for establishing the diagnosis of cancer in 41 patients.

With the increasing age of the population, the incidence of diverticulosis and its complications will become greater. Diverticula most often involve the sigmoid colon, and we agree with Mayo and Delaney[1] that over 90% of the complications arise in this area. Carcinoma is frequent in the sigmoid colon as well. In a previous study, we[2] found that of 355 patients with carcinoma of the colon, exclusive of the rectum, 21% had both diverticula and carcinoma. In 10% both lesions were located in the sigmoid flexure. Because of these facts, we elected to study the problem of differential diagnosis of these lesions, which are becoming increasingly more important in an aging population. We feel that a certain danger in coexistence of diverticula and carcinoma lies in the attitude of physicians, radiologists, and surgeons toward diverticula. There is an inclination on the part of some observers to disregard the finding of diverticula as being relatively unimportant; yet we found that in 10% of our

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From the Department of Surgery, Henry Ford Hospital.

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patients with carcinoma of the sigmoid, diverticula were present as well. The danger of carcinoma being overlooked while a more obvious diverticulitis is treated is ever present, and, hence, the need to reevaluate the diagnostic aids is apparent.

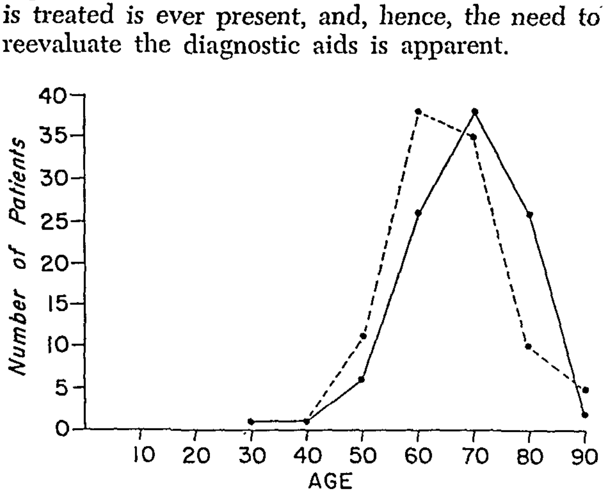

Fig. 1.—Distribution of carcinoma (*solid line*) and diverticulitis (*broken line*) in 100 patients.

Patient Data

Material.—This study is based on data from 100 patients with proved carcinoma of the sigmoid and 100 patients with every reasonable finding supporting the diagnosis of diverticulitis. These patients were investigated between the years 1953 and 1957. The final proof that the lesion was carcinoma came from the pathologist. Biopsy of the lesion through the sigmoidoscope, or the resected specimen itself, provided tissue for microscopic examination. Clinical investigation, sigmoidoscopic examination, barium enema examination and, in several instances, the surgical specimen provided the basis for the diagnosis of diverticulitis. Patients with carcinoma of the descending colon above the sigmoid and carcinoma of the rectum were omitted from this study since they do not present the same problem in diagnosis.

Age and Sex.—In an analysis of the age grouping we can see from figure 1 that most of these patients with sigmoid carcinoma and diverticulitis are between 40 and 80 years of age. Figure 1 clearly illustrates the similarity of the ages in the two groups. The age of the patient is of no assistance in making the differential diagnosis. Youth does not preclude tumor, and Graham[3] reported two carcinomas in patients of 27 and 34 years of age respectively. Diverticula should never be taken lightly, because carcinoma can be hidden in the same segment of colon. As for sex distribution, both diseases were more prevalent in men (fig. 2). However, this was of no differential diagnostic value in arriving at the correct diagnosis.

Symptoms.—There was a difference in the symptoms, as shown in table 1. Certain complaints merit further consideration. Change in bowel habits, bleeding, pain, and weight loss are four of the most important symptoms. Welch[4] pointed out that symptoms caused by cancer tend to be steadily progressive, while those of diverticulitis are intermittent. Constipation and bleeding were more common and more prominent complaints in patients with carcinoma than in those with diverticulitis. This is in keeping with the nature of the lesion. Carcinoma here is annular and constricting and may well interfere with the passage of formed feces. Ulceration is much more common in patients with carcinoma, hence the bleeding.

Bleeding per rectum is a treacherous complaint and must never be taken lightly. The patient's interpretation of the cause and quantity of bleeding is deceptive and misleading, because he may wish to minimize the gravity of this complaint. Some of the patients' phrases descriptive of this complaint include: "occasionally noted blood in the stool," "bleeding from hemorrhoids," "passed blood once two years ago," "passed a few flecks of blood," and "passed a teaspoonful of blood once," and finally there is the modest patient who reports that he never inspects his stool. Bleeding occurs frequently in patients with carcinoma and we are inclined to accept the incidence of 64% reported by Colcock and Sass.[5] Bleeding from diverticula has been variously reported as being rare, by Jones,[6] occurring in 2%, by Fallis,[7] and occurring in 15%, by Welch and co-workers.[8] Noer[9] recorded bleeding in 20 of 68 cases of diverticulosis-diverticulitis.

Pain is always a dominant complaint in patients with inflammatory lesions. This study has convinced us that pain, when prominent, strongly suggests diverticulitis. This is of particular value when the pain is recurrent. In general, about twice as many patients with diverticulitis will have pain (continuous, intermittent, or recurrent) as will a similar group of patients with sigmoid carcinoma. The pain is located in the left lower abdominal quadrant, lower part of the abdomen, or throughout the abdomen, depending on the extent of the inflammatory involvement.

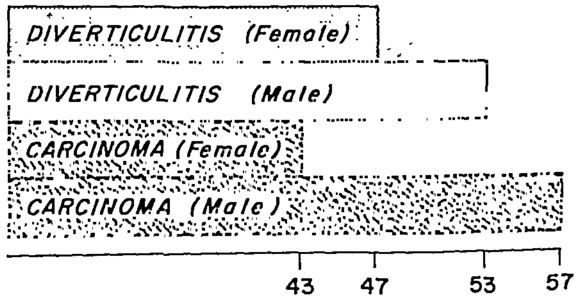

Fig. 2.—Sex distribution in patients with diverticulitis and carcinoma. Figures indicate number of patients in each group.

Finally, a word of caution: carcinoma may perforate and can produce a picture indistinguishable clinically from diverticulitis. Weight loss was seen in 50% of patients with carcinoma of the sigmoid, but sigmoid diverticulitis caused weight loss in only 17% of these patients.

We were impressed with the fact that urinary tract symptoms were present in approximately 20% of patients with either lesion. Frequency of urination, dysuria, urgency, and nocturia were the common complaints. The proximity of the sigmoid lesion to the bladder may be a possible explanation for these symptoms.

Signs.—Obesity is nearly twice as common in patients with diverticulitis as in those with sigmoid malignancy (table 1). Fever is also more frequent in patients with diverticulitis. Sixty-five per cent of these patients showed temperature elevations, while 30% of those with sigmoid neoplasms had comparable findings.

Tenderness on palpation was elicited consistently in patients with the inflammatory lesions. Of these patients 93% had some degree of pain on palpation. This is a significant finding and suggests diverticulitis, but the experienced observer will not overlook the possibility that a carcinoma may be present, as well. Adding to the confusion, 37% of the patients with carcinoma also had tenderness on physical examination.

We were disappointed in the findings elicited by palpation. Inflammation resulted in tenderness, so that effective palpation could not be carried out in many cases. Furthermore, lesions located in the sigmoid may not be of sufficient size to be palpated by the examiner, either abdominally or rectally.

Table 1.—*Distribution of Signs and Symptoms in 100 Patients*

	Disease	
	Diverticulitis, %	Carcinoma, %
Symptom		
Constipation	57	71
Diarrhea	18	31
Diarrhea alternating with constipation	11	18
Bleeding	25	68
Continuous pain	61	33
Intermittent pain	64	31
Recurrent pain	71	53
Mass discovered by patient	5	5
Urinary tract symptoms	28	20
Weight loss	17	50
Sign		
Fever	65	30
Tenderness	93	37
Mass		
Abdominal	10	24
Rectal	9	16
Pelvic	25	16
Obesity	40	21
Miscellaneous signs		
Fistula	4	...
Perforation	5	1
Intestinal obstruction	7	15
Ileus	26	4
Anemia	2	10
Leukocytosis (more than 10,000 wbc/cu.mm.)	50	23

Intestinal obstruction (cramping, abdominal pain, vomiting, distention, and decreasing bowel movements) was more common in patients with carcinoma of the sigmoid (table 1). Of patients with carcinoma of the sigmoid 15% showed this finding, whereas only 7% of patients with diverticulitis had a comparable sign. Ileus (abdominal pain, vomiting, distention, decreased bowel movements, and a silent abdomen) was more common in patients with diverticulitis. Of patients studied 26% with the inflammatory lesion showed adynamic ileus. Complete obstruction, which is refractory to treatment, is most strongly suggestive of malignancy and is a finding of real differential diagnostic value. Diverticulitis is likely to cause ileus because of inflammatory involvement of not only the colon but the small intestine as well. Such complications as fistulas, perforation, and sinus tract were much more common in patients with diverticulitis in this study.

Table 2.—*Sigmoidoscopic Findings in Patients with Diverticulitis and Carcinoma of the Sigmoid*

	Patients with Diverticulitis, %	Patients with Carcinoma of Sigmoid, %
Carcinoma seen	.	57
Negative findings	91	41
Blood	6	41
Polyps	5	12
Narrowing, angulation, spasm (12-15 cm.)	18	7

Diagnostic Tests

Laboratory Data.—Consistent studies of the blood supported the statement that leukocytosis is commonly observed in patients with sigmoid diverticulitis whereas anemia is seen more often in patients with carcinoma in the same location.

Sigmoidoscopic Findings.—We believe that sigmoidoscopy will have more to offer in the future. First, we hope to take advantage of a longer sigmoidoscope, and at present we are using a longer instrument in selected cases. Improvements in the sigmoidoscope should be forthcoming. In addition, we believe that the suggestion of Wisseman and co-workers[10] should be followed and cytological studies should be done on smears taken at sigmoidoscopy.

In patients with proved cases of carcinoma of the sigmoid, the lesion was seen through the sigmoidoscope in 43% (table 2). Actual bleeding, or recognizable blood, was seen on sigmoidoscopy in 41% of patients with proved sigmoid carcinoma. This finding is indeed noteworthy. In a previous study involving similar cases, we found that the sigmoidoscopic examination successfully revealed the presence of carcinoma in 57% of cases. Therefore, it seems reasonable to conclude that in proved cases of carcinoma of the sigmoid it is possible to visualize the lesion in about one-half of the cases.

In patients with diverticulitis of the sigmoid, the sigmoidoscopic examination may reveal little. We have been disappointed in the positive information obtained by sigmoidoscopy. Although Willard and Bockus[11] had seen only one diverticulum in a 10-year period, a negative examination may be reassuring. Unusual tenderness, angulation, narrowing, and spasm may suggest diverticulitis, but carcinoma can produce all of these findings as well. Tenderness may be marked in patients with diverticulitis. Blood is not commonly seen in these patients, compared to those with carcinoma. We believe that the actual visualization of blood at the time of sigmoidoscopy is of definite value and strongly suggests malignancy.

The positive diagnosis of diverticulitis cannot often be made with the sigmoidoscope. Rarely, a diverticular opening may be seen, or, still more rarely, pus may be seen discharging from such an orifice. We must depend on some other diagnostic aid to make the diagnosis of sigmoid diverticulitis. We will not repeat the roentgenologic differential diagnostic points between diverticulitis and carcinoma here, since they have been summarized by Rowe and Kollmar.[12] Diagnostic errors occur, as Golden[13] has pointed out, because of failure to realize that (1) diverticula may not fill; (2) either lesion can cause complete obstruction; and (3) an infectious granuloma which destroys the mucosa cannot be differentiated from carcinoma by roentgenologic examination.

Table 3.—*Results of Barium Enema Examination in Patients with Diverticulitis and Carcinoma of the Sigmoid**

	Patients with Diverticulitis, %	Patients with Carcinoma, %
Diverticulosis	77	28
Diverticulitis	29	8
Sinus tract	3	...
Fistulous tract	4	...
Perforation	5	...
Polyps	...	4
Spasm	12	...
Carcinoma	2	68
Possible carcinoma	...	16
Undecided	5	...

* Totals are greater than 100%, since multiple observations were made on several individual examinations.

Barium Enema Examination.—We found that the barium enema examination resulted in the correct diagnosis in 68% of patients with carcinoma of the sigmoid. In addition, the diagnosis was suggested in another 16%, making the correct, or presumably correct, diagnostic total 84% of patients with carcinomas. In explanation of these figures, it is reasonable to point out that some of these lesions were quite small and others were associated with polyps (table 3). In a previous study of similar cases we observed that the barium enema examination yielded a correct diagnosis of carcinoma in 65% of proved cases. Barium enema examination in patients with diverticulitis resulted in the diagnosis of diverticulosis in 77% and diverticulitis in 29% (table 3).

Complications of diverticulitis can best be demonstrated by roentgenologic examination. The significance of the roentgenologic report of diverticulosis must be interpreted by the clinician. He has the evidence of temperature elevation, pain, leukocytosis, and localized or generalized tenderness. Whenever the radiologist sees narrowing in the sigmoid, he may report spasm or make his report of diverticulitis. The radiologist sees the result of prolonged inflammation or its complications. Whenever there is doubt as to the nature of the lesion, after careful study, surgery is advisable. The greatest diagnostic accuracy in lesions of the sigmoid, either neoplastic or inflammatory, is obtained by careful barium enema examination.

Surgical Diagnosis.—The surgeon at the operating table may be unable to arrive at the correct diagnosis. Diverticulitis may produce an indurated, fixed lesion, involving not only the sigmoid but adjacent viscera such as the bladder and small intestine as well. Carcinoma, if it is complicated by perforation and subsequent inflammation, may produce an identical operative picture. Before examining the specimen, the surgeon was uncertain about the correct diagnosis in 18% of these cases; nonetheless, the correct treatment was used and the sigmoid was resected in all questionable cases.

Pathologist's Report.—Once the pathologist finds the more serious lesion of carcinoma, he is not likely to spend time describing diverticula. The pathologist referred to the diverticula accompanying the carcinoma in only 10 of the 100 specimens.

Diverticulitis was treated surgically in 21 instances. In each case surgery was necessary because of complications. Of 14 resected specimens all were found to contain diverticula accompanied by severe inflammatory changes.

Summary and Conclusions

In summarizing the value of the various clinical findings in the differential diagnosis between sigmoid carcinoma and sigmoid diverticulitis in this series of 100 patients, it can be suggested that constipation (71%), bleeding (68%), weight loss (50%), abdominal mass (24%), intestinal obstruction (15%), and anemia (10%) point to carcinoma. Tenderness (93%), recurrent pain (71%), fever (65%), constipation (57%), leukocytosis (50%), obesity (40%), and ileus (26%) strongly suggest diverticulitis. Fistulas and perforation involving the sigmoid are much more common in patients with the inflammatory lesion.

The sigmoidoscopic examination is of definite value in establishing the diagnosis of carcinoma of the sigmoid. In about 50% of patients a positive diagnosis can be made through the use of the sigmoidoscope; in this series sigmoidoscopy revealed carcinoma in 41%. It is of little value in making the positive diagnosis of diverticulitis, however.

The barium enema examination is a valuable aid in making the diagnosis, not only of carcinoma but of diverticulitis as well. The correct, or presumably correct, diagnosis of carcinoma was made in 84% of these cases, 68% being definitely demonstrated and 16% assumed to be demonstrated. Diverticula were reported in all patients with diverticulitis studied, and diverticulitis was suspected in 29. The barium enema examination is indispensable to the diagnosis of diverticular disease.

The surgeon at the operating table cannot always make the differentiation between sigmoid carcinoma and diverticulitis. In 18% of patients studied in this report there was uncertainty about the correct diagnosis until after the lesion had been removed and opened. In this group of patients the accepted procedure of wide resection of adjacent areas of vascular and lymphatic drainage is advocated. When there is doubt, an operation of the type performed for cancer should be done.

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DIVERTICULITIS OF CECUM AND ASCENDING COLON

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In the course of about 5,000 examinations of the colon, diverticula have been noted in 10 cases. Five of the 10 patients had diverticulitis, and surgery became necessary in three of these. The operation consisted of hemicolectomy in two patients, a man 49 and a woman 42 years of age. In the third patient, a man 73 years of age, the preoperative symptoms and findings were those of acute appendicitis, but laparotomy revealed multiple diverticula of the cecum and ascending colon in the presence of a normal appendix. The experiences here cited show that diverticulitis is likely to escape diagnosis unless it is watched for, and they illustrate the value of roentgenographic methods of examination in the differential diagnosis between diverticulitis and appendicitis.

Roentgenologic methods of investigation are a valuable complement to clinical examination in the diagnosis of diverticulitis of the cecum and of the ascending colon. Without roentgenographic information, an erroneous diagnosis of appendiceal disease often is made, which results in inappropriate treatment. It is the purpose of this paper to review the available pathological and roentgenologic information concerning diverticulitis of the right side of the colon and to describe a limited experience of the role of the radiologist in diagnosis.

Incidence

Prior reports suggest that diverticulitis of the cecum and of the ascending colon is not an unusually rare clinical entity. Potier[1] reported its occurrence in a 32-year-old woman as early as 1912. During the period from 1912 to 1947, only 100

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cases of diverticulitis of the right side of the colon, almost all of which had been surgically diagnosed, were reported in the literature. In the ensuing five years, however, more than 50 additional cases were collected and added by Lauridsen and Ross.[2] By 1959, the total should exceed 300, including those reported by Greaney and Snyder[3] in 1957. This rapid increase indicates that heightened awareness of the existence of this disease has brought about a steady increase in its recognition.

Various authors have reported that the presence of diverticula was demonstrated in the cecum and in the ascending colon in only 0.7 to 1.5% of all patients with colonic diverticulosis.[4] The material subsequently to be reported suggests that this incidence may be significantly higher. Men and women are affected with about equal frequency. This is in sharp contrast to the situation in cases of colonic diverticular disease on the left side, in which men outnumber women in a ratio of at least two to one. Generally, diverticulitis of the cecum and of the ascending colon is said to occur in a younger age group than the generalized and left-sided forms. The difference in age is accounted for by the high percentage of congenital diverticula occurring in the region of the cecum.

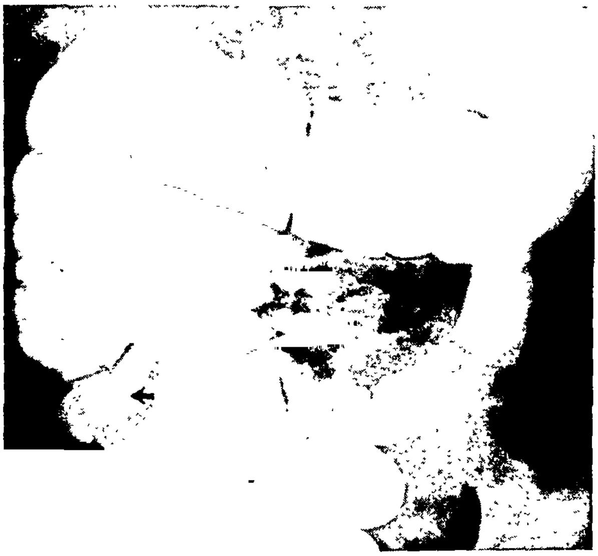

Fig. 1.—Solitary cecal diverticulum. Barium mixture fills colon and outlines rounded cavity superimposed on cecum in frontal projection (*arrow*).

Anatomic Considerations

Colonic diverticula may be divided into the true, or congenital, and the false, or acquired, types. In the true type, all of the muscle layers of the outwardly extending colonic wall are present, while in the acquired type there is a herniation of the mucosa and submucosa through a defect in the muscular coat.[5] Lauridsen and Ross[2] found that more than 70% of the cases reviewed represented true diverticula.

Most solitary cecal diverticula probably are congenital. Retention of the embryologic "transient appendix" has been suggested as the basis for the formation of a solitary cecal diverticulum.[6] The structure is an outgrowth from the cecal tip, and it occurs in the embryologic development of the hindgut, which enlarges during the 6th week of fetal life and normally atrophies toward the end of the 7th week. Solitary diverticula of the cecum and of the ascending colon are said to occur within a segment 2 cm. above or below the level of the ileocecal junction in most instances[7] (fig. 1). The anterolateral border of the cecum is the most frequent location, followed by the posteromedial border.[2]

The false or acquired type of diverticulum commonly is multiple and is found most often in the sigmoid area, but it can occur anywhere in the colon between the ileocecal valve and the rectum (fig. 2). Such diverticula are thought to result from intraluminal pressure on potentially weak areas, where blood vessels pierce the muscular coat of the intestinal wall.[8] Multiple cecal diverticula most often are of the acquired type and usually are associated with diverticula elsewhere in the colon, although they may occur in isolation.

Clinical and Pathological Aspects

Patients with acute diverticulitis of the right side of the colon commonly present a clinical picture of acute intra-abdominal inflammatory disease, and most often a diagnosis of appendicitis or appendiceal abscess is made. In only 6% of patients undergoing operation in a large series studied by Anderson[4] had the disease been correctly diagnosed preoperatively. A history of previous attacks which spontaneously subsided and a finding of a palpable mass in the right lower quadrant should be interpreted as indications of the possibility of diverticulitis. A history of prior appendectomy is helpful, if present, but was found to be infrequent in the reports surveyed by Nissenbaum and co-authors.[9]

At exploratory laparotomy, the operative findings usually fall into one of two categories. The first may be a hidden or intramural inflammation when the entire length of the diverticulum lies within the wall of the cecum or of the ascending colon. In the second, there is a distinct projection beyond the intestinal wall, which is grossly evident to the surgeon. The first infection begins in one diverticulum, presumably after obstruction of its outlet and stasis. In most surgically excised diverticula suppuration is present, and, with the development of an abscess, a mass is produced which may be grossly indistinguishable from carcinoma, particularly in the case of the solitary intramural type of diverticulum.[10] As reported by Lauridsen and Ross,[2] enteroliths were found in 55% of 104 patients in whom pathological studies had been carried out.

Nonoperative treatment often is successful when the diagnosis of acute diverticulitis of the cecum or of the ascending colon is established both clinically and by roentgenographic examination. When no preoperative diagnosis has been made, the decision as to proper therapy must be made by the surgeon at the operating table. Generally, surgical procedures should be limited to simple diverticulectomy or inversion of a solitary diverticulum and to the treatment of complications of diverticulitis.[11] A conservative approach to surgery is indicated because of the tendency of diverticulitis to subside spontaneously.[12] Resection of the cecum and colectomy on the right side sometimes are necessitated by the surgeon's inability to distinguish between an inflammatory mass, which originates in a diverticulum, and a perforating carcinoma; however, with use of more extensive operative procedures, both morbidity and mortality are increased significantly.[13]

Roentgenologic Investigation

Routine roentgenologic examination by means of a plain survey film of the abdomen is widely accepted as good medical practice in the diagnosis of acute abdominal disease. This procedure is considered worthwhile in inflammatory conditions, although the possibility of accurate diagnosis of a lesion, such as diverticulitis, by this method is remote. While most of the diverticula on the right side contain enteroliths, few enteroliths calcify sufficiently to be seen in a plain abdominal roentgenograph.[14]

The best opportunity for correct diagnosis of diverticulitis of the right side of the colon is provided by administration of a barium enema. The use of such a procedure in acute abdominal inflammatory conditions must be accompanied by exercise of clinical judiciousness, inasmuch as administration of a barium enema ordinarily is contraindicated in the presence of acute appendicitis. The use of the barium enema is considered more practical in the presence of subacute, recurrent, and chronic infection. While Wolf[15] reported no untoward effects from barium enema, including double-contrast examination, it is noteworthy that all of his patients had subsiding infections.

In contrast to diverticula of the left side of the colon, those on the right tend to have wider and shorter necks, which may be confused with sacculations between eccentric haustra. One of the most characteristic [illegible] features of diverticulitis, well [illegible],[15] is a localized, discrete, eccentric intramural indentation of the barium-distended intestine. The overlying mucosa is intact, although edematous, and transverse folds are often crowded together. As with diverticulitis elsewhere, the junction of the involved area with adjacent normal intestine is gradual and smooth, without a shelving margin. The involved portion of intestine often is fixed, and a large area adjacent to it may exhibit inflexibility and limited distensibility.

The presence of a pericecal mass as a result of abscess formation has been emphasized by Nissenbaum and co-authors[9] and is said to occur in one-third of patients. The extrinsic pressure produces an irregular defect in the outline of the cecum, as contrasted with a focal indentation of the caput with appendiceal disease.[15]

The offending diverticulum usually does not fill with barium; if it is of the solitary type, diagnosis depends on a high index of suspicion and the recognition of secondary changes. When adjacent diverticula are outlined in the roentgenograph, the correct diagnosis is more readily apparent. A diverticulum containing an enterolith may appear as a ring shadow rather than as a budlike projection from the colon.[16] The appendix, when present, often fills with barium; whereas, in appendiceal disease, filling of the appendix is rare.[15]

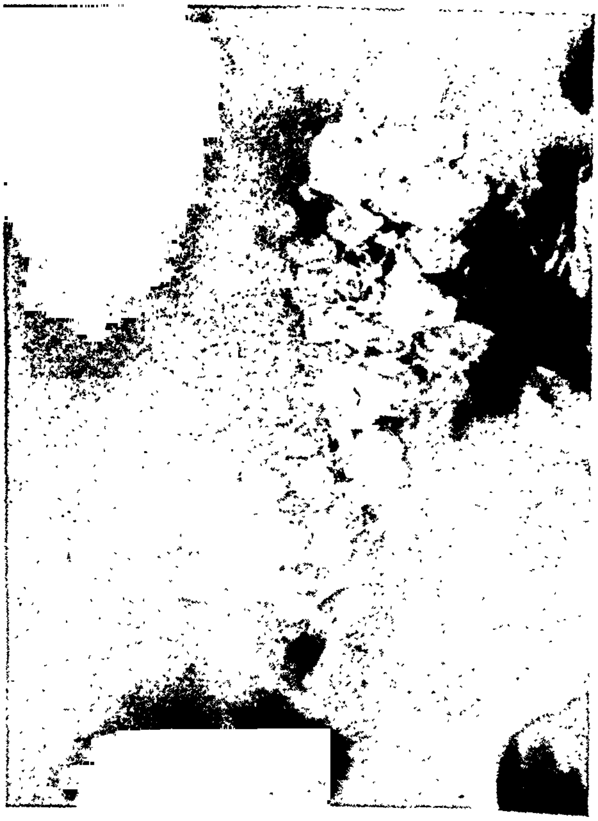

Fig. 2.—Multiple cecal diverticula. Postevacuation film after barium enema demonstrates host of diverticula largely confined to cecum and ascending colon.

Report of Cases

At the North Carolina Memorial Hospital, during the course of about 5,000 colon examinations, 10 patients have been encountered in whom diverticula involving only or predominantly the right side of the colon were present. Of three patients who were operated on (see table) and who will be described, two (cases 1 and 2) had developed an inflammatory mass secondary to perforation of a diverticulum (fig. 3). The third patient (case 3) showed evidence of present and past inflammation, without perforation or abscess formation (fig. 4). Two other patients (cases 4 and 5) exhibited convincing clinical and roentgenographic evidence of acute di[illegible] tis of the right side of the colon. Under conservative management the inflammation subsided, and operation was not performed.

Case 1.—A 49-year-old man was admitted to the hospital because of abdominal pain in the right lower quadrant of seven days' duration. On examination, a poorly defined, firm, tender mass was palpated, somewhat laterally, in the right lower quadrant of the abdomen. A plain roentgenographic film of the abdomen showed normal findings.

Features of Interest in Five Patients with Diverticulitis of Right Side of Colon*

Case No.	Roentgenographic Impression	Operative Findings and Treatment
1	Appendiceal abscess	Mass, cecal area, neoplasm not excluded; hemicolectomy
2†	Diverticulitis with abscess	Diverticulitis with pericecal inflammatory mass; hemicolectomy
3	Diverticulitis of cecum (postoperative barium enema)	Localized diverticulitis of cecum; appendectomy
4	Diverticulitis of cecum	Nonoperative treatment‡
5	Diverticulitis of cecum and ascending colon	Nonoperative treatment‡

* Average age 54.8 yr.

† Patient had previous appendectomy.

‡ Both patients receiving nonoperative treatment were asymptomatic on discharge.

On the day after admission, a barium enema was given; the roentgenographic film revealed irritability of the cecum and a smooth filling defect on the medial and posterior surface near the cecal tip, corresponding to the palpable mass. The roentgenographic and clinical preoperative diagnosis was appendiceal abscess.

Two days after admission, exploratory laparotomy was performed. The appendix was normal. A large mass was found, involving the posterior wall of the cecum and the retrocecal area. The surgeon's impression was that neoplastic disease was a strong possibility, and he elected to carry out a hemicolectomy on the right side, with end-to-end anastomosis of the terminal part of the ileum and the middle part of the transverse colon.

Pathological examination disclosed a retrocecal abscess, secondary to perforation of a solitary cecal diverticulum. No fecalith was present in the diverticulum.

Case 2.—A 42-year-old woman was admitted to the hospital because of abdominal pain, which had begun suddenly three weeks previously and initially had been in the epigastrium. On the fifth day of her illness, the pain moved to the right lower abdominal quadrant and subsided to such a degree that only "soreness" was described. During the next 10 days she had anorexia, fatigue, and the discomfort in the right lower quadrant continued. Her pertinent medical history included appendectomy, excision of an ovarian cyst, and hysterectomy.

On examination there was slight tenderness in the epigastric and suprapubic regions and marked tenderness in the right lower quadrant of the abdomen, with associated guarding and a poorly defined mass. The white blood cell count was 16,000 per cubic millimeter.

A barium enema roentgenogram revealed many diverticula in both the distal descending and the sigmoid colon, with diverticula scattered proximally as far as the ascending colon. The medial wall of the cecum showed an extrinsic pressure effect, which suggested pericecal abscess. The cecal tip was not deformed (fig. 3).

A preoperative diagnosis of diverticulitis of the ascending colon, with rupture and local abscess formation, was made. At laparotomy there was a mass 7 cm. in diameter in the mesentery at the junction of the cecum and the ascending colon, intimately attached to the wall of the colon, secondary to perforation of a diverticulum into the mesentery. The surgeon elected to perform a hemicolectomy on the right side, with end-to-end anastomosis of the terminal part of the ileum and the right side of the transverse colon.

Pathological examination of the specimen revealed that several of the diverticula led into areas of dense scarring and adhesions in the mesentery. Histological examination of one of the diverticula showed an intact smooth muscle layer and the submucosa and smooth muscle surrounding the diverticulum were diffusely infiltrated with lymphocytes, plasma cells, and eosinophils.

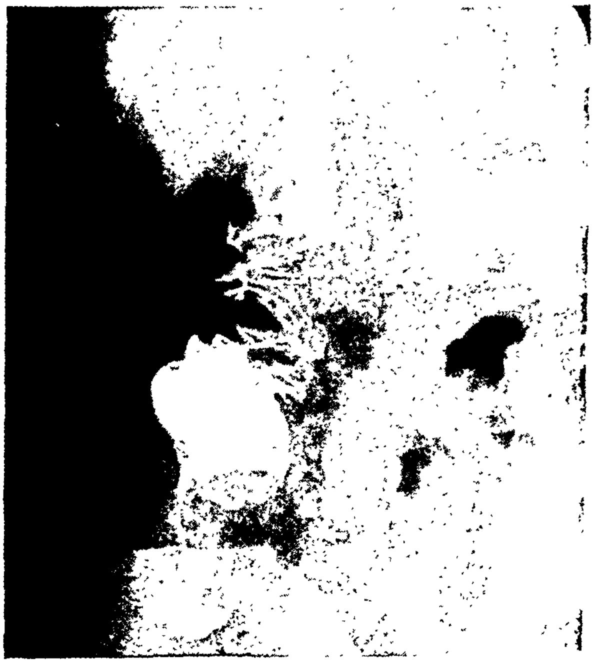

Fig. 3. (case 2).—Pericecal abscess resulting from perforated diverticulum. Postevacuation film after barium enema reveals contraction of cecum and gross edema of mucosal pattern which remains intact. On the medial aspect an extrinsic pressure effect is present, produced by abscess (arrow). Cecal tip is smooth and relatively spared, with no deformity in region of base of appendix.

Case 3.—A 73-year-old man was admitted to the hospital with a complaint of pain in the lower part of the abdomen of 18 hours' duration. At onset, the pain had been vague and continuous, but later it had become intermittent and cramping. Anorexia, nausea, and vomiting had supervened, and the pain became localized to the right lower quadrant of the abdomen.

On examination, the patient's temperature was 100.1 F (38.39 C). There was tenderness and increased muscle tone on the right side in the lower part of the abdomen. The white blood cell count was 15,500 per cubic millimeter.

A diagnosis of acute appendicitis, possibly retrocecal, was made. At operation, the appendix exhibited no evidence of acute inflammation, but there were multiple diverticula of the cecum and of the ascending colon. The cecum showed thickening and considerable scarring, which indicated previous inflammation, and the surgeon considered the diagnosis of diverticulitis to be obvious. Eleven days after operation a barium enema was given; the roentgenographic film revealed numerous diverticula throughout the colon and several large diverticula in the region of the cecum (fig. 4).

Case 4.—A 71-year-old woman was admitted to the hospital because of pain in the right flank of three weeks' duration. On abdominal examination, moderate tenderness in the right upper quadrant, the right flank, and the right lower quadrant was noted, but no mass was palpable. Several stool specimens were positive for occult blood but later became negative.

A barium enema roentgenogram revealed several diverticula of the ascending colon, just above the ileocecal junction; the appendix filled normally. It was felt that low-grade diverticulitis of the ascending colon was the probable explanation of the pain and the occult blood in the stools. The patient was discharged as asymptomatic after eight days' observation and was placed on a medical regimen which included instructions to follow a low-residue diet.

Case 5.—A 39-year-old man was admitted to the hospital because of cramping epigastric pain which had awakened him several hours prior to admission. The pain increased in severity and became constant.

There was a history of recurrent abdominal pain, and an upper gastrointestinal series that had been carried out seven months prior to admission was normal. A plain roentgenographic film taken two days later showed irregular collections of barium in the right side of the abdomen, which denoted diverticula of the colon.

On examination, the patient's temperature was 101 F (38.33 C), and his pulse rate was 100 per minute. Tenderness and muscle spasm were found in the epigastrium and in the right side of the abdomen. A provisional diagnosis of diverticulitis, with perforation, and local peritonitis was entertained, and a conservative therapeutic regimen consisting of parenteral feeding, administration of antibiotics, and symptomatic measures was instituted. The patient's clinical state improved steadily, and, when he had become relatively asymptomatic, a barium enema was administered. The roentgenographic film revealed multiple diverticula in the region of the ascending colon, without evidence of acute inflammation at that time. The patient was discharged symptom free and was advised to follow a low-roughage diet.

Of the other five patients not reported here in detail, one had extensive diverticulosis of the entire colon, including the terminal part of the ileum. There was a history of repeated colonic bleeding but no pain. It is felt that inflammation, by production of ulceration of a diverticulum or diverticula, can be presumed to be the cause of bleeding. This case was not included in the reports because there were no definite localizing signs pointing to the right side of the colon. Another patient with colonic bleeding had diverticulosis of the entire colon and a mass in the right side of the abdomen. Coexisting disease elsewhere, however, precluded operative investigation of the colon.

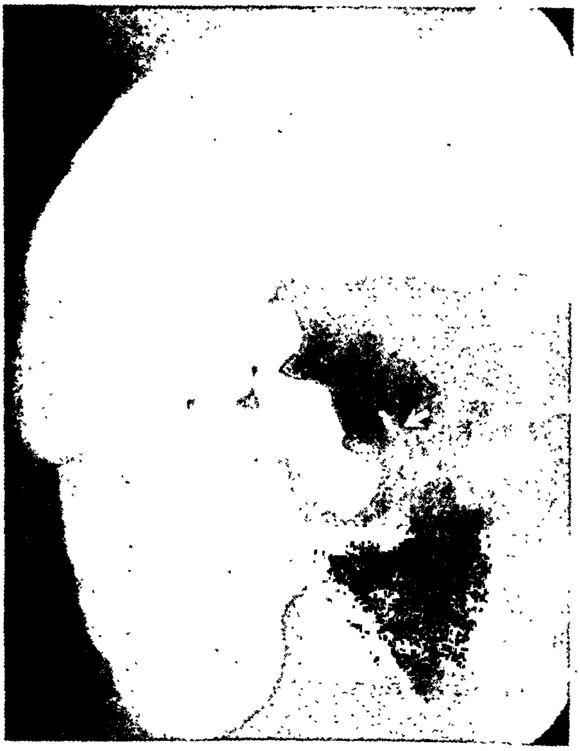

Fig. 4. (case 3).—Unusually large diverticulum of medial side of cecum. Barium mixture from proximal portion of colon enters and partially fills 6-by-2.5-cm. outpocketing attached by a wide neck just above ileocecal junction. Curvilinear barium shadow (*arrow*), which partially outlines wall of diverticulum, usually appears as result of radiolucent enterolith encircled by contrast medium.

One patient had multiple diverticula along the right side of the colon, and another had a solitary cecal diverticulum, but neither had clinical evidence of diverticulitis. In a final instance the patient's presenting complaint was chronic diarrhea. Diverticula were found to be confined to the ascending and the sigmoid colon. There was a transient episode of lower abdominal pain on the right side, but there was no definite evidence that this was due to diverticulitis on the right side.

Two pathological specimens were available for study as a result of the resections performed on the patients in cases 1 and 2. In case 3, only the appendix was excised. No enterolith was found in the diverticulum in either instance. In one specimen, histological examination revealed that the infected diverticulum was of the true type.

Comment

The five patients with diverticulitis that have been presented include three surgically proved and two clinically probable instances of acute diverticulitis of the cecum and of the ascending colon. Of the three patients who were operated on, the clinical diagnosis was appendiceal abscess in one and acute appendicitis in one, and a correct diagnosis of diverticulitis with abscess was made in the third. The two conservatively treated patients presented a clinical and roentgenographic picture that was entirely consistent with the diagnosis of diverticulitis, and they responded satisfactorily to a nonoperative regimen.

In two of the three patients operated on the disease was correctly diagnosed at operation. In the third, hemicolectomy was performed because of an erroneous suspicion of neoplastic disease. In one patient whose disease was correctly diagnosed, hemicolectomy was performed because of the extensive nature of the diverticular disease.

Preoperative barium study of the colon was carried out in two of the three patients operated on (cases 1 and 2). In one (case 2) the barium enema helped to establish the correct diagnosis. In the second the roentgenographically demonstrated extrinsic pressure defect in the cecum was interpreted as being due to appendiceal abscess (case 1). In one instance (case 3), the barium enema was performed postoperatively.

For one patient (case 4), the finding of diverticula of the right side of the colon at barium enema was a strong factor in the decision against exploratory laparotomy. On another occasion (case 5), diverticula had been suspected on the basis of a 48-hour abdominal roentgenographic film after performance of an upper gastrointestinal series, and nonoperative treatment was carried out because of this information. After clinical improvement, a barium enema roentgenogram confirmed the presence of diverticula.

According to our own review of previous reports and the review of the literature given by Nissenbaum and co-authors,[9] the experience described in the five case reports here presented is significant in that the roentgenologist played an important role in the diagnosis in four patients. Previously most patients used to be subjected to postoperative roentgenographic studies to define the extent of the disease process diagnosed at the operating table. The more frequent judicious use of roentgenographic examinations preoperatively should lead to improved results through accurate diagnosis and the avoidance of unnecessary surgical procedures.

Summary

An increased awareness of the existence of diverticulitis of the right side of the colon has brought about more frequent recognition of this disease. Because of the similarity of symptoms and signs, the clinical differentiation of diverticulitis from appendicitis or appendiceal abscess is difficult. Roentgenologic methods of examination, especially the judicious use of the barium enema, provide means for more accurate preoperative diagnosis in diverticulitis of the right side of the colon. In the group of patients described, roentgenographic diagnosis was an important consideration in decisions regarding treatment.

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OSTEOCHONDROSIS OF CAPITAL EPIPHYSIS OF FEMUR (LEGG-CALVÉ-PERTHES DISEASE)

LONG-TERM END-RESULTS IN NINETY PATIENTS

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The course of osteochondrosis of the epiphysis of the head of the femur has been studied in 76 boys and 14 girls, many of them followed up as long as 25 years after completion of treatment. It is agreed that weight-bearing must be prevented during the initial period of destruction of the femoral head, but there is disagreement as to how it can best be prevented and how soon it can be resumed during the period of regeneration. In any individual patient these two periods were essentially equal in duration. The average duration of symptoms before admission was 7 months, 24 days; the average age of the patients at admission was 7 years, 10 months. In patients over the age of 8 years the end-result was poor, regardless of the type of treatment. In the youngest patients, with early diagnosis, the end-results were excellent provided weight-bearing was prevented. The most effective of the methods tried for the restriction of weight-bearing was bed rest with Buck's extension.

Disturbance of the epiphysis of the head of the femur resulting in aseptic changes has been described under a number of names and synonyms. This relatively common condition was described by four physicians in four different countries within a period of two years. Each of these physicians described the same pathological condition of the epiphysis of the femoral head, but each listed the process under a different descriptive term. Arthur T. Legg[1] of Boston presented his findings in 1909, with publication of his paper occurring in February, 1910. Jacques Calvé,[2] a French orthopedist, described this condition to medical groups on several occasions in the years 1908 and 1909, but his paper was not published until July, 1910. Georg Perthes of Germany published the report of his collected cases in late 1910. Henning Waldenström of Sweden published a paper in 1909 in which he described the condition in a differential discussion of other juvenile pathological processes of the hip.

In the succeeding 25 years numerous authors published papers mentioning the terms Perthes disease, Perthes-Calvé disease, Calvé-Perthes disease, Legg disease, Calvé disease, or Legg-Calvé-Perthes disease. The two most commonly accepted descriptive terms for this condition are osteochondritis deformans coxae juvenilis and coxa plana. Many writers now list this entity as Legg-Calvé-Perthes disease. Regardless of which generic, eponymous, or pathological descriptive term is used, this condition of aseptic necrosis of the epiphysis of the head of the femur is seen frequently enough to deserve a high index of suspicion on the part of all physicians.

Until the definite etiology of Legg-Calvé-Perthes disease is known, little can be added to the voluminous literature on this perplexing condition. None of the suggested etiologies has withstood critical appraisal.[3] There is no general agreement as to the ideal method of treatment of this condition. The various advocates of operative, nonoperative, ambulant, and recumbent types of treatment all report end-results which vary to such a degree that it is difficult to arrive at any definite conclusions about the best way to treat this condition. The one factor of agreement that is apparent in the literature is that non-weight-bearing on the affected femoral head is essential until revascularization of the capital femoral epiphysis occurs. Disagreement exists, however, as to how to best prevent weight-bearing during the period of destruction of the femoral head.[4] Disagreement also exists as to when weight-bearing may be resumed. Some authors advocate resumption of weight-bearing at the first roentgenographic evidence of regeneration of the femoral head. Others feel that restriction of weight-bearing is essential until there is complete regeneration of the capital femoral epiphysis. The practitioner treating a patient with this condition must be well versed in the interpretation of roentgenograms and capable of deciding when the destruction of the femoral capital epiphysis has ceased and regeneration has begun.

Case Materials

This paper consists of the clinical impressions of a review of 90 cases of Legg-Calvé-Perthes disease. The patients were all treated at Crippled Children's

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Hospital, and the impressions are based on the interpretation of roentgenograms of patients many years after completion of treatment. A number of the earlier patients treated have now reached adulthood, and roentgenograms of these patients were obtained through the cooperation of orthopedists and radiologists in the localities throughout the country where these persons now reside. No attempt has been made to compare one type of treatment with another. We have arrived at certain conclusions after reviewing these cases which we feel are significant in the future evaluation of cases of this disease.

The 90 patients included 76 boys and 14 girls, a 5:1 ratio of males to females. To properly evaluate these patients as to their treatment and end-result, we have arbitrarily allocated each case to one of three groups, depending on the appearance of the capital femoral epiphysis at the time of beginning of treatment. Group 1 (30 patients) consists of those patients with minimal destructive changes at the time of admission; group 2 (36 patients) of those with moderate destructive changes; and group 3 (24 patients) of those with advanced destructive changes on admission. None of the 90 patients had received any definitive treatment prior to admission to the hospital. The average duration of symptoms of all patients prior to admission was 7 months and 24 days; the average age of patients was 7 years, 10 months. This latter figure is somewhat high, due, we believe, to the delayed diagnosis of many of the earlier cases treated.

The primary purpose of this paper is to emphasize the importance of early diagnosis of this condition, if a good end-result is to be obtained. Many of the patients treated earlier had had hip or knee pain and a limp for over a year prior to admission. We compared the average duration of symptoms of the patients treated prior to 1948 with the average duration of symptoms of the patients treated since that time and determined that in the latter group the symptoms had existed for only four months prior to admission. This, of course, is an improvement, and it is our hope that this figure can be reduced even further in the future. The ideal, for patients with this disease, would be for all cases to be in group 1, those with minimal epiphysial changes at the time of admission.

To attempt to compare each of these groups with the type of treatment employed and evaluate the end-results obtained would be to repeat results reported in previous studies. Rather than make such comparative conclusions we offer the following impressions, which we believe not only are pertinent to this study of osteochondrosis of the capital epiphysis of the femur but are applicable to all cases of this disease.

Case Impressions

All patients with minimal early changes (group 1) had an excellent end-result. All patients given a diagnosis at the age of 5 years or earlier had an excellent end-result. All patients given a diagnosis over the age of 8 years had a poor end-result, regardless of the type of treatment used. It is probably of some significance that all patients over the age of 8 at the time of diagnosis were in group 3 (those with advanced destructive changes). All of the patients in group 3 had a poor end-result, regardless of the type of treatment. In this group of 90 cases, restriction of weight-bearing was best accomplished by bed rest and the use of Buck's extension. This method of treatment is admittedly expensive and, except in the instance of an exceptionally cooperative patient and parents, must be carried out in a hospital. We were not impressed with the value of the ischiatic weight-bearing brace as a means of preventing weight-bearing. A number of patients in this study showed flattening and other changes in the proximal femoral epiphysis when permitted ambulation with use of an ischiatic weight-bearing brace. The use of the Perthes' sling and crutches[5] has proved satisfactory in a small number of these patients, but complete cooperation between the physician, the patient, and the parents is essential if this form of ambulation is to be satisfactory and prevent weight-bearing on the affected leg.

The patients treated by spica cast immobilization did as well as those treated by Buck's extension. With plaster immobilization the degree of muscle atrophy of the involved leg was marked, but this disappeared completely within six months after resumption of weight-bearing. It was noted that in every patient in this series there was some degree of temporary shortening of the involved leg during the period of recumbency. The shortening lasted up to as long as two years after resumption of full activity. This, we believe, was merely a temporary physiological shortening, secondary to atrophy of disuse. In the cases which healed, with an essentially normal femoral head, there was not one instance of residual shortening. All patients with residual extensive changes in the femoral head had femoral shortening up to as much as 1.9 cm.

In evaluating the individual roentgenograms of these patients, we have been impressed by the fact that, in any individual patient with this disease, the period of regeneration of the femoral head will be essentially equal in length to the period of femoral head destruction. In the final evaluation of what constitutes an excellent end-result in patients with Legg-Calvé-Perthes disease, the roentgenographic appearance of the femoral head must be considered the critical point of evaluation. An essentially normal-appearing femoral head in the patient's late adolescence or early adulthood constitutes an excellent end-result. With this measure of evaluation it has been impressive to us that early diagnosis, plus complete absence of weight-bearing during this period of capital epiphysial destruction, will accomplish a satisfactory end-result. Certainly a high index of suspicion on the part of all physicians will result in the early diagnosis of this condition. The individual orthopedist must use the method of restriction of weight-bearing which in his hands produces the best end-result.

The period of recumbency or non-weight-bearing is widely variable, depending on the age of the patient and the appearance of the femoral head at the time of diagnosis. The point at which weight-bearing may be resumed depends on the experience of the orthopedist with this condition and must be based on his opinion that weight-bearing will not be harmful to the femoral head.

Summary

A review of 90 cases of osteochondrosis of the capital femoral epiphysis (Legg-Calvé-Perthes disease) was based on an evaluation of the roentgenographic appearance of the affected femoral head up to as long as 25 years after completion of treatment.

If an essentially normal-appearing femoral head is the desired end-result, then diagnosis must be made early, before the destructive changes in the proximal femoral epiphysis have brought about irreversible structural changes from weight-bearing. Early age, plus early diagnosis, plus absence of weight-bearing will give an excellent end-result. In the patients over the age of 8 years the end-result was poor, regardless of the type of treatment. The most effective method of restriction of weight-bearing in these cases was by means of bed rest and Buck's extension.

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EARLY RECOGNITION OF OSTEOCHONDROSIS OF CAPITAL EPIPHYSIS OF FEMUR

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A comparison was made between 54 patients with osteochondrosis of the capital femoral epiphysis and 25 with synovitis of the hip. All of the former group limped, 51 had restricted hip motion, and 48 complained of pain. All of the patients with synovitis limped also, 21 had restricted hip motion, and 19 complained of pain. The two entities were clinically indistinguishable except that roentgenographic findings were characteristic in osteochondrosis and recovery from it was slower. Of the 25 patients with synovitis, 22 ultimately became asymptomatic after treatment with bed rest with light traction. The remaining three later developed osteochondrosis. It is likely that synovitis predisposes the patient to osteochondrosis or is the first stage in its development. Therefore children with clinical, but without roentgenologic, evidence of hip disease should be watched for signs of osteochondrosis of the capital femoral epiphysis.

Osteochondrosis of the capital epiphysis of the femur (Legg-Calvé-Perthes disease) is a disease of the hip in young children that is characterized by necrosis, followed by a regenerative process that is variable and conditioned by the age of the patient, the adequacy of treatment, and the rapidity with which it is instituted. Reports of end-results have established that prolonged avoidance of weight-bearing (often for two or more years) on the affected extremity, until healing has occurred, is the best available treatment capable of restoring normal function. Yet, even after adequate treatment, the late end-results are all too frequently bad, with the result that this disease is responsible for a significant proportion of the hip disease and disability encountered in adults.

Ratliff,[1] reviewing 41 treated patients with osteochondrosis of the capital femoral epiphysis, with an average follow-up period of 17 years, reported 18 with good, 15 with fair, and 8 with poor results. Mindell and Sherman [2] found 13 unsatisfactory results in 46 treated patients whose progress was followed for up to 15 years. Stamp and co-workers,[3] reviewing 102 treated patients, reported 50

From the Hospital for Special Surgery.

with satisfactory, 28 with fair, and 24 with poor results, with follow-up periods of 8 to 12 years. Evans,[4] reviewing 54 treated patients, with an average follow-up period of 10 years, found 15 with good, 21 with fair, and 16 with poor results. Thus, in a reported total of 243 adequately treated patients with osteochondrosis of the capital femoral epiphysis, slightly more than 50% (125 patients) were found to have poor or fair results when their progress was followed into early adult life.

The results after treatment are generally considerably better in those patients treated early in the course of the disease. Early recognition of this disease is, therefore, of decided practical importance. Unfortunately, in most instances, there is a substantial time lag between the onset of symptoms and the initial diagnosis. Many children continue to bear weight during the period of active bone necrosis, when the avoidance of epiphysial compression could obviate the flattening and deformity of the femoral epiphysis that otherwise invariably results. A review of the literature, as well as of my own series of cases, reveals an average delay in diagnosis of six months. It is proposed that this time lag, the result in part of parental procrastination and in part of inadequate medical evaluation, is the principal reason for the high proportion of unsatisfactory results despite diligent treatment. A thorough awareness of the clinical features of this disease is an essential prerequisite to its early diagnosis; it is principally to that end that this paper is written.

Review of Cases

During the decade 1948 to 1958, 54 patients with osteochondrosis of the capital femoral epiphysis were admitted to the Hospital for Special Surgery. There were 46 boys and 8 girls, ranging in age from 2 to 12 years. The average age at the onset of symptoms was 5 years; 45 patients were aged 7 years or less. The duration of symptoms prior to diagnosis ranged from two days to 29 months and averaged 5 months. There were nine patients with bilateral hip involvement. Of interest is the fact that eight of these patients had complaints referable to only one side, and in two this was in the hip that, roentgenographically, appeared less involved. It is wise, therefore, to examine both hips at all times.

The chief symptom, common to all patients, was limp; 48 patients complained of pain, which was referred to the hip or groin in 18; the knee in 19; the lower thigh in 10, and throughout the extremity in 3. Night cries were prominent in 20 cases. The two principal physical signs were limp (54 cases) and restricted hip motion (51 cases). The chief components of hip motion affected were internal rotation (41 cases), external rotation (32 cases), abduction (24 cases), adduction (16 cases), and extension (10 cases). Hip contracture (attitude change of the extremity) was present in 21 patients, consisting of flexion, external rotation, and abduction in varying combinations. Thigh atrophy, averaging 0.5 in., was found in 17 cases, and shortening of the affected extremity was present at the time of diagnosis in 14. The latter is largely the result of flattening of the femoral head.

Differential Diagnosis

The symptoms and signs of osteochondrosis of the capital femoral epiphysis are not characteristic of that disease alone. Early pyogenic and tuberculous hip disease, although increasingly infrequent, may pose a problem in differential diagnosis. Occasionally, it may be necessary to resort to biopsy of the femoral head. In all of my patients with this disease, complete blood counts, determinations of sedimentation rate, urinalysis, and tuberculin and agglutination tests were routinely performed but found to yield normal results.

The commonest cause of hip pain in children today is said to be so-called transient synovitis, an apparently nonspecific, self-limiting, inflammatory process. Wiles[5] estimated it to be responsible for four of five cases of hip pain in children. A review of the literature reveals many synonyms, including "transient coxitis," "phantom hip," "transitory epiphysitis," and "observation hip." Infection, allergy, and, particularly, trauma has each been considered a possible causal factor.

The age incidence and clinical features of synovitis of the hip closely parallel those of early osteochondrosis of the capital femoral epiphysis. The two entities are clinically indistinguishable except for the usually rapid recovery in the former condition and the characteristic roentgenographically visible changes associated with the latter. (Soft tissue changes, visible on x-ray examination to the trained observer, may substantiate the presence of synovitis, but they are inconstant.) The diagnosis of "transient synovitis" is, therefore, one that should preferably be made by hindsight. To accept it as a working diagnosis, as has been advocated,[6] is to run the risk of underestimating the inherent seriousness of hip pain in children. This was further emphasized after a study of patients admitted to this hospital with a diagnosis of synovitis of the hip.

Review of Cases of Synovitis of the Hip.—Twenty-five patients with synovitis of the hip were admitted to the Hospital for Special Surgery from 1948 to 1958. Many more with this disease passed through our clinics but were not hospitalized; it is difficult to follow the progress of these patients. The patients hospitalized included 14 boys and 11 girls, ranging from 3 to 12 years of age. The average age at the onset of symptoms was 5 years and 7 months; the average duration of symptoms prior to diagnosis was five weeks. A history of antecedent trauma was obtained in only eight cases.

Limp was present in all cases, and 19 patients complained of pain, which was referred to the hip or groin in 15 and to the knee in 4. Restriction of hip motion was observed in 21 cases; the same components were affected as in osteochondrosis of the capital femoral epiphysis. Hip contracture (attitude change of the extremity) was manifested by 15 patients. Thigh atrophy was present in three cases and shortening of the affected extremity in two.

The diagnostic procedures used in patients with osteochondrosis were used in these patients with synovitis and found to give normal results. Aspiration of the hip joint was carried out in five cases; the resultant fluid exhibited no abnormality on smear or culture.

The treatment in each case consisted of complete bed rest with light traction. A gradual return to normal activity was permitted after disappearance of all symptoms and signs. Eighteen patients became asymptomatic after bed rest for periods ranging from 4 to 28 days. Three of the remaining patients required additional confinement to bed for a total of seven weeks because of persistent complaints. One patient required treatment for 15 weeks before becoming symptom-free.

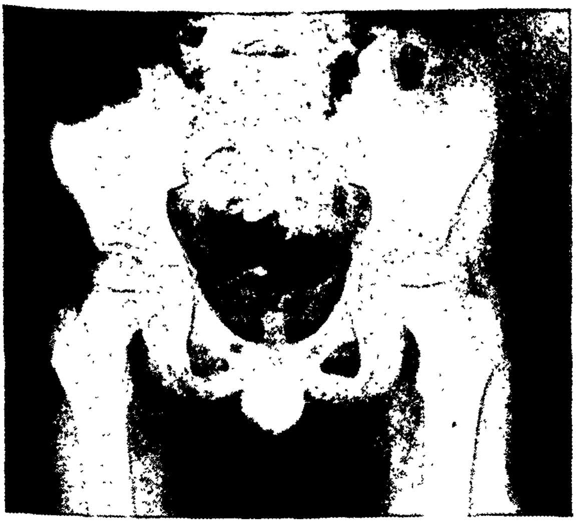

Fig. 1 (case 1).—Roentgenogram of hip made on first visit, Aug. 30, 1955.

Further follow-up information is available in 14 cases, for periods ranging from 26 months to eight years. Of these patients 10 made a complete and uncomplicated recovery without recurrence. One patient has 1.5 in. of shortening in the affected extremity after three years of follow-up examinations. The remaining three patients developed osteochondrosis of the capital femoral epiphysis; their case histories follow.

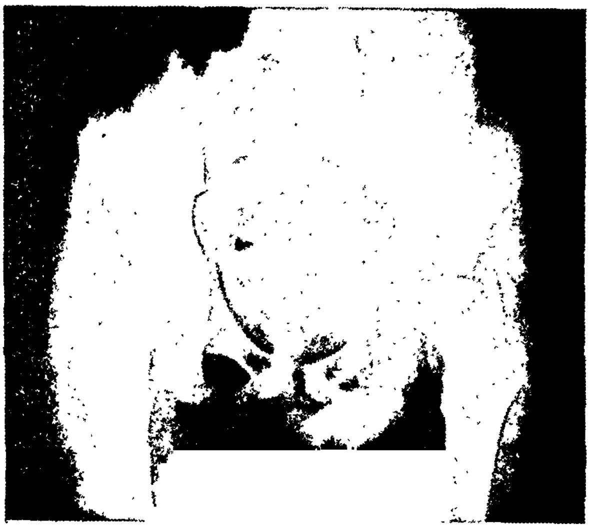

Fig. 2 (case 1).—Roentgenogram of hip made Nov. 15, 1955. Note marked flattening and density of left femoral epiphysis, with large lucent area laterally.

Case 1.—A 7-year-old boy was first seen in clinic with a two-week history of limp. The left leg was observed to be held in more external rotation than the right, but hip motion was felt to be unrestricted and the patient denied pain. X-ray examination of both hips revealed normal findings (fig. 1). A diagnosis of synovitis of the left hip was made and the patient was permitted to return home, with instructions to restrict his activities. At a second examination one month later, weakness of left hip abduction was observed and the patient was thought to have a mild case of poliomyelitis. About three months after his initial visit, the patient returned with a more pronounced limp and pain in the left groin. When he was examined there was marked restriction of left hip motion and a flexion contracture of 15 degrees. X-ray examination now revealed the changes of osteochondrosis of the capital femoral epiphysis (fig. 2).

Case 2.—A 7-year-old boy was first seen in the clinic with a 10-week history of limp and pain in the left hip. The left leg was seen to be held in excessive external rotation and slightly abducted, and there was restriction of internal rotation at the hip. X-ray examination of both hips showed nothing abnormal. The patient was hospitalized with a diagnosis of "idiopathic synovitis."

Treatment consisted of complete bed rest with traction to the affected leg. Diagnostic procedures revealed no abnormality. The patient was [illegible] tom-free after eight days of treatment and was discharged shortly thereafter, with full weight-bearing. The pain and limp recurred one week after his return home and were still present when he was seen in clinic three weeks later. At this time, with the exception of the limp, no abnormal signs were observed and both hips were again found to be normal on x-ray examination. The child was permitted to return home and advised to rest in bed, but he returned to clinic one month later with the same complaints. On this occasion, examination revealed marked restriction of left hip rotation and x-ray examination revealed the characteristic changes of osteochondrosis of the capital femoral epiphysis.

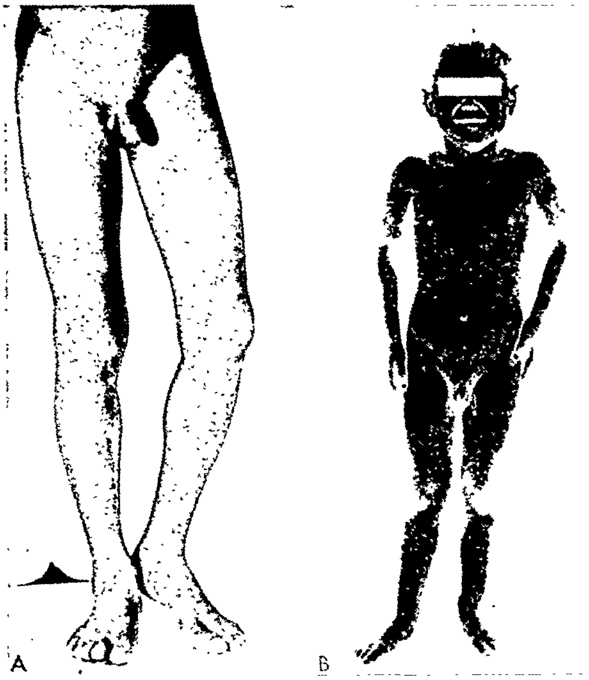

Fig. 3.—*A*, typical deformity seen in severe synovitis or osteochondrosis of capital epiphysis of femur (external rotation, abduction, flexion). *B*, more subtle deformity (external rotation of right leg) seen in milder synovitis of hip and early osteochondrosis.

Case 3.—A 3-year-old girl was first seen in clinic with an 18-month history of limp and pain throughout the right leg. The leg was held in more external rotation than the opposite extremity, but there was *no restriction* of *hip motion* and the child denied pain when examined. Both hips were normal on x-ray examination.

The patient was seen on 13 occasions during the ensuing two years because of intermittent limp and pain in the right leg which she could never accurately localize. Night cries were frequent. Repeated examinations were recorded as revealing no abnormality, but no additional roentgenograms of the hip were obtained. More than two years after her initial clinic visit, at the age of 5 years, the patient was brought to hospital with severe pain throughout the right leg. Examination at this time revealed a flexion-external rotation contracture of the right hip with considerable restriction of motion. Roentgenograms showed the changes of far-advanced osteochondrosis of the capital femoral epiphysis, with marked deformity of the femoral head, which persisted after six years of follow-up investigation.

Comment

In this series of 54 patients with osteochondrosis of the capital femoral epiphysis only 3 were given a correct diagnosis prior to attending the clinic. Previous medical attention had been sought in at least 26 cases, and among the diagnoses made were rheumatic fever, flatfoot, knock-knee, synovitis of the hip, sprained hip, and behavior problem (one patient was referred to a psychologist). Roentgenograms of the hip had been obtained in 10 of these cases and showed normal findings. It may be assumed that hip disease was not seriously considered in the remaining cases. The interval between the onset of symptoms and the diagnosis of the disease averaged eight months for those children who had received early medical advice, compared to an average of five months for the entire series. It would appear that the assumption of a benign diagnosis at the onset may afford either the parents or

Chief Clinical Features of Synovitis of Hip and Osteochondrosis of Capital Femoral Epiphysis

	Osteochondrosis of Capital Femoral Epiphysis	Synovitis of Hip
Patients, no.	54	25
Male	46	14
Female	8	11
Average age at onset, yr.	5.0	5.6
Average duration of symptoms, mo.	5	1.3
Limp, %	100	100
Restricted hip motion		
No.	51	21
%	94	84
Internal rotation, no.	41	17
External rotation, no.	32	8
Pain		
No.	47	19
%	87	76
Site		
Knee, no	19	4
Hip or groin, no.	18	15
Thigh, no.	10	...
Attitude change		
No.	21	15
%	39	60
Thigh atrophy		
No.	17	3
%	31.5	12
Shortened extremity		
No.	14	2
%	26	8

the doctor, or both, comfort enough to delay seeking additional advice. Other published reports[7] reveal a similar unfortunate time lag in diagnosis.

The natural history of osteochondrosis of the capital femoral epiphysis is well illustrated by the three case histories presented. It should be noted that at the initial examination each of the patients manifested limp and an attitude change (external rotation) of the affected extremity. These two signs are practically pathognomonic of acute inflammatory hip disease. Typically, the hip is held in flexion, external rotation, and abduction (fig. 3*A*). In this position the joint is better able to accommodate the raised intra-articular tension. Failure to observe an early attitude change (fig. 3*B*) and the frequency with which pain is referred away from the hip, to the knee or thigh, undoubtedly contribute to many delayed diagnoses.

There are grounds for the belief that synovitis is the earliest manifestation of osteochondrosis of the capital femoral epiphysis and that it is possibly an important contributing factor in its development. These include the natural history of the disease and the closely similar clinical features of the two entities (see table). Furthermore, marked synovial reaction, out of proportion to the bony changes, has been observed at operation in patients with early osteochondrosis. It is possible that severe synovitis, with the attendant rise in intra-articular tension, may serve to compress the blood supply to the femoral head. This concept would explain the occasionally encountered case of osteochondrosis of the capital femoral epiphysis that appears to be completely or partially aborted by early diagnosis and treatment.

It is proposed that patients thought to have synovitis of the hip should be watched carefully for the development of this osteochondrosis. Normal x-ray findings, as has been shown, are insufficient to rule out this disease with finality. These patients should be treated by avoiding weight-bearing until all clinical features have resolved. Fortunately, in most instances, the synovitis will subside rapidly with restriction of activity. The return to normal activities should be gradual, with the recurrence of symptoms necessitating additional complete bed rest and greater caution. On the basis of present knowledge of the natural evolution of this disease the progress of these patients should be followed at no more than monthly intervals for three to six months. Such an approach should aid materially in the earlier recognition of this disease and thereby improve the over-all results of treatment, and, if a causal relationship between synovitis and osteochondrosis of the capital femoral epiphysis does exist, it might also significantly reduce the incidence and severity of an otherwise serious disease.

Conclusions

In studying two series, 54 patients with osteochondrosis of the capital femoral epiphysis (Legg-Calvé-Perthes disease) and 25 with synovitis of the hip, the principal clinical features of acute hip joint disease here seem to be pain, restricted motion, and contracture or attitude change. In young children, most cases of hip pain are due to synovitis and, with less frequency, to osteochondrosis. The excessive interval that invariably exists between the onset of symptoms and the diagnosis of this disease reduces the opportunity for a good end-result even after adequate treatment. This interval may be reduced by the careful evaluation of limp and pain in the hip (or knee) in children. The referral of pain to the knee or thigh should serve to attract rather than distract attention from the hip joint. It is wise to examine both hips at all times.

The diagnosis of "transient synovitis" should be made by hindsight. Children with clinical, but without roentgenologic, evidence of hip disease should be regarded as having potential or incipient cases of osteochondrosis of the capital femoral epiphysis until proved otherwise. The possibility of there being a causal relationship between synovitis and this osteochondrosis is a reasonable hypothesis. Persistence of the synovitis and variations in the vascular supply to the femoral head are probably factors which determine whether or not this osteochondrosis will develop.

Drs. T. C. Thompson and W. Graham aided in the preparation of this report. Mrs. O. Fischer supplied the photographs and roentgenograms.

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CURRENT STATUS OF GRISEOFULVIN

REPORT ON ONE HUNDRED SEVENTY-FIVE CASES

Leon Goldman, M.D., Jan Schwarz, M.D., Robert H. Preston, M.D., Amanda Beyer, M.D.
and
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Griseofulvin, an antibiotic, was used in treating diseases of the skin in 175 patients with various types of ringworm infection. The largest single group consisted of 22 patients who took griseofulvin by mouth in doses of 250 to 500 mg. four times a day for treatment of tinea corporis caused by Trichophyton rubrum. In this group of 22, 3 patients were cleared of lesions, 8 improved, 1 was somewhat relieved, and 10 had not taken the drug long enough for evaluation. A group of four patients with tinea capitis caused by Microsporum canis were cleared of all lesions by taking 250 mg. by mouth four times a day for four to eight weeks. Among the 84 who took the drug by mouth, only 9 reported side-effects, and these were neither serious nor lasting. In some of the 91 patients who received the drug topically complete clearing of the skin lesions was achieved. Topical administration is important for tinea pedis, since oral administration of griseofulvin for this condition gave erratic results.

The history of griseofulvin has been an interesting one. Griseofulvin was isolated in 1939 by Oxford and associates [1] from Penicillium griseofulvum dierckx but was discarded because it failed to show the antibacterial activity hoped for from the various penicillin derivatives under study at that time. For the next eight years this substance received no further attention. In 1947 Brian [2] reported on a substance that he isolated from Penicillium janczewski, which he called the "curling factor" because it resulted in abnormal development of fungal hyphae; that is, the hyphae shriveled and became stunted under the effect of this material (fig. 1). Later that year, Grove and McGowan [3] identified griseofulvin and the "curling factor" as the same substance. In the years that followed, griseofulvin was used extensively against fungous disease in plants, such as tomatoes, beans, and mushrooms, and in the treatment of ringworm in cattle. Despite these developments, however, no attempt was made to use griseofulvin for the treatment of fungous infections in human beings. In fact, as late as July, 1957, at a conference held in London [4] on fungous diseases and their treatment, no mention of this compound was made, although antifungal antibiotic agents were discussed.

Use of Griseofulvin in Human Subjects

The effectiveness of griseofulvin against fungi in both plants and animals eventually led Gentles and associates to explore the possibility of using this antibiotic in the treatment of the hitherto virtually intractable ringworm infections in human subjects. To this end, Gentles [5] studied the effect of griseofulvin against experimentally induced ringworm in guinea pigs and demonstrated its value in these conditions; later, Gentles and associates [6] were able to recover orally administered griseofulvin from the hair of guinea pigs and thereby prove that this substance was absorbed from the gastrointestinal tract and incorporated into newly growing cells.

Gentle's work soon was followed by worldwide studies in human subjects afflicted with ringworm infections. Among the first to subject griseofulvin to clinical trials were Pardo-Castello and associates [7] who began using this compound in 1957 with a high degree of success. However, the first investigator to report on the use of griseofulvin in human subjects was Riehl [8] who, in November, 1958, described the high activity of this compound against dermatophytes in 15 patients with ringworm infections. Riehl's work was followed rapidly by further successful studies in human subjects by Williams and associates,[9] Blank and Roth,[10] Goldman,[11] Riehl [12] himself, and Sulzberger and Baer.[13] The use of griseofulvin has been studied also in patients with fungous infections other than ringworm, such as moniliasis (candidiasis), North American blastomycosis, histoplasmosis, actinomycosis, torulosis (cryptococcosis), and pityriasis (tinea) versicolor. It has proved to be inactive in all of these conditions and also in mycetoma due to Mucor, in our experience.

Clinical Studies

Since the beginning of 1959 our group has had griseofulvin under study in more than 175 patients. Although treatment has not been completed in all of these cases, and the eventual outcome therefore is not known, it was decided to make a report, at this time, of 175 cases of our series because of the potentially widespread application of griseofulvin and the consequent need for a fuller understanding of this compound.

From the Department of Dermatology of the College of Medicine of the University of Cincinnati and the Laboratory of Mycology, Cincinnati General Hospital and Jewish Hospital.

Our initial observations confirm the previously cited studies in that they show griseofulvin to be almost uniformly effective against the group of conditions known as ringworm infections: tinea capitis, tinea barbae (barber's itch), tinea corporis (tinea circinata or tinea glabrosa), tinea cruris, dermatophytosis (tinea pedis, athlete's foot) and onychomycosis (tinea unguium). Griseofulvin exerts a fungistatic, not fungicidal, effect on the following micro-organisms responsible for these infections: Trichophyton gypseum (mentagrophytes, interdigitale), rubrum (purpureum), schoenleini, sulfureum, tonsurans, and verrucosum; Epidermophyton floccosum; and Microsporum audouini, canis (lanosum), and gypseum (fulvum).

Among the gratifying clinical features of early evidence of response to orally given griseofulvin is the rapid objective and subjective improvement of lesions of the scalp and the glabrous skin. Patches of infection, even in cases due to T. rubrum, perhaps the most resistant ringworm pathogen, rapidly become more comfortable, perspiration improves, kerion of the scalp promptly begins to subside, and itching ceases. However, in spite of these early signs of improvement, relatively prolonged treatment is necessary to achieve clinical eradication of the offending organisms. Therefore, one should not become discouraged in those cases in which few or no signs of improvement appear in the first two weeks after institution of therapy. It should be pointed out that improvement is particularly slow in areas of thick skin, such as in palms and soles, and slowest when the nails are involved, especially the toenails, which may take up to six weeks before showing initial response.

Diagnostic Procedures.—Because a number of conditions, such as psoriasis, leprosy, syphilis, parapsoriasis, dermatitis seborrheica, moniliasis, intertrigo, alopecias,[13] and bacterial infections, which of course are not sensitive to griseofulvin, may masquerade as fungal conditions in view of their similar appearance, it is vitally important that an accurate and definite diagnosis be established before griseofulvin is prescribed.

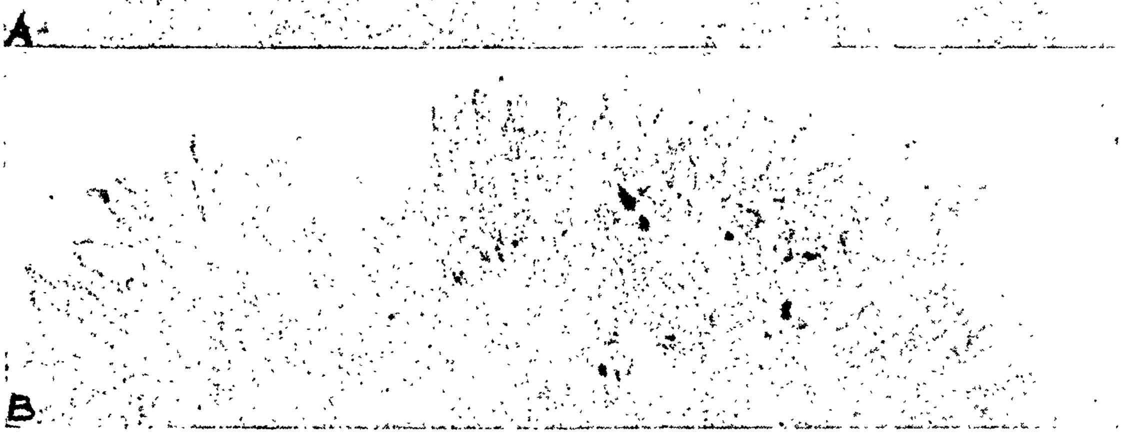

Fig. 1.—Microsporum canis. *Top,* normal growth in medium. *Bottom,* griseofulvin in medium showing "curling effect" on fungus.

For the purpose of such a diagnosis, we routinely take scrapings from marginal scales or from the roof of a full vesicle in an untreated area; then, a portion of these scrapings is used for direct mounting with a 10% potassium hydroxide solution for microscopic examination after at least 20 minutes has elapsed, and the remainder is placed in a sterile test tube and after 48 hours transferred for culture in an appropriate medium (fig. 2). Positive cultures may not always be obtained when the nails are involved. However, special biopsy techniques with Gridley's stain will show fungus elements in the nail plate. Such cases with definitive or, as we believe, presumptive diagnosis generally will respond to griseofulvin. In tinea capitis due to M. audouini or M. canis we also use the Wood's light as a diagnostic tool, since hair infected with these fungi will fluoresce under it. If local facilities are not available, the practitioner can place the scrapings in an envelope and mail them to an experienced medical mycology laboratory or the department of dermatology of a medical center.

With the availability of an effective antiringworm agent, the establishment of adequate training programs in mycology for laboratory technicians acquires even greater importance than heretofore.

Therapeutic Regimen.—In conformity with currently available data, griseofulvin is administered daily in oral doses of 250 mg., three or four times per day, except in T. rubrum and some T. mentagrophytes infections, which may require higher dosages. Children generally respond to one-half of the adult dosage. Treatment is continued until two weeks after scrapings from the affected structures prove negative for the presence of fungi both on direct microscopic examination and on culture.

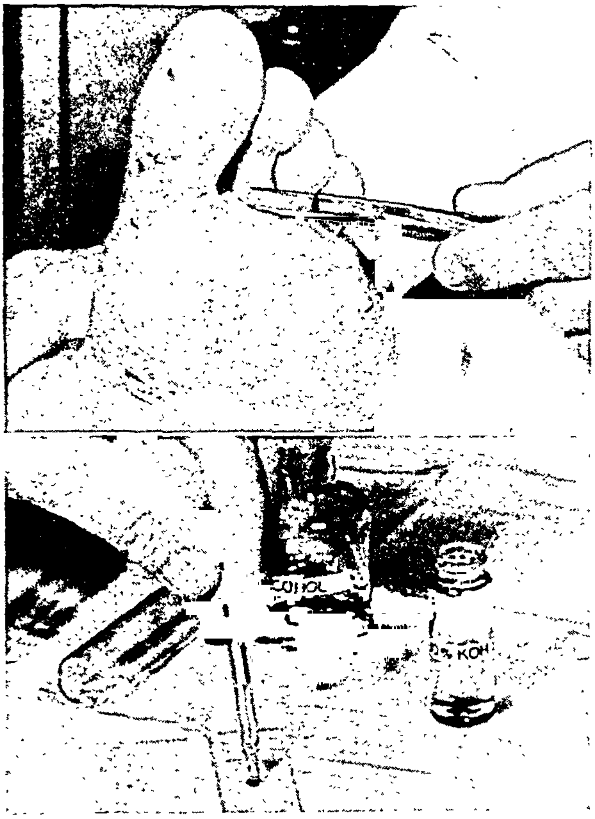

Fig. 2.—*Top*, method of obtaining skin for culture in severe tinea pedis. Alcohol has been used on skin and allowed to dry thoroughly before removal of scales. *Bottom*, technique for simple preparation of direct mount. Thoroughly dried scales are covered with 10% potassium hydroxide solution and allowed to stand for 20 minutes before examination.

Duration of treatment varies according to the affected area. Infections of the hair and the glabrous skin usually require from two to eight weeks of treatment, with some cases necessitating even more prolonged treatment. In infections located in areas of thicker skin, such as in palms and soles, we found that therapy may have to be continued for four to eight weeks, while onychomycosis requires from four to six months of therapy, with a few extensive or unusually resistant cases necessitating even more prolonged administration of griseofulvin. Several different dosage schedules are currently under study by various groups, including ourselves. Among the possibilities under consideration is that the permanence of griseofulvin in keratin may permit intermittent regular-dosage or even single-dosage therapy with amounts of 5 Gm. of griseofulvin.

Since fungi are not dependent on living structures for survival, we recommend that infected clothing be avoided to prevent possible reinfection and contamination of others; this is particularly true of hats, socks, stockings, and perhaps shoes. In cases of tinea capitis we advise that the hair be covered with the usual protective cap and be clipped close or shaved weekly whenever possible, but definitely at the end of the third week of treatment. Mild antiseptic ointments may be used. In patients with onychomycosis nails should be kept short. Since secondary yeast infections with Candida albicans may occur, especially in intertriginous areas, adequate local measures should be taken. It is an interesting fact that griseofulvin may also relieve the carrier state of tinea pedis temporarily.

Because the use of griseofulvin in human subjects is relatively new and there are few data on its possible toxicity in long-term programs, we take special precautions with our patients, and we believe that these precautions should be observed until additional studies with this compound, currently being conducted by dermatologists and other specialists, are completed. Complete blood counts are taken at two-week intervals, especially during prolonged therapy and after administration of the single large doses. While we have not seen any changes in the blood picture, Pipkin [14] has reported some temporary depressions in the white blood cell count. Patients are instructed to report instances of sore throat, fever, or other abnormal manifestations. Although some investigators, including ourselves, have given griseofulvin to known penicillin-sensitive patients without untoward manifestations, the possibility of cross-sensitivity with this penicillin derivative cannot be completely ruled out. In fact, we have used investigative topically administered griseofulvin in a patient with tinea pedis who had severe penicillin eruptions at the time; griseofulvin did not interfere with the course of this penicillin reaction. Studies with the Schultz-Dale technique and, perhaps, with the penicillin-sensitized red cell technique may be advisable.

Occasional instances of drug rashes, in the form of urticarial, vesicular, and maculopapular eruptions, have been observed; these reactions were not severe and seldom required discontinuance of treatment. Rare cases of headache have occurred, and the possibility of neurotoxicity is currently being studied. We have done pretreatment electroencephalographic studies and repeated this examination during intervals of therapy. The results were negative in three patients, two had no complaints, and one had severe headaches two days after taking griseofulvin. While we have given griseofulvin to patients with gastrointestinal ulcers without any difficulty, others have noted reactivation of a long-standing colitis. We have observed one patient with bloody diarrhea.

Paget and Walpole [17] have observed interference with mitosis in actively dividing cells, especially with spermatogenesis, after intravenous and intraperitoneal administration of extremely high doses (200 mg. per kilogram of body weight) of griseofulvin to rats. This phenomenon has not been observed in human subjects. In fact, Blank and Roth [10] and others have carried out periodic sperm counts in a number of patients and found no deviations from the normal. To resolve this question definitely, MacLeod and Nelson are carrying out a large-scale study involving weekly sperm counts and testicular biopsies in patients under prolonged therapy with orally administered doses of griseofulvin. Initial results of this study show no adverse effects on spermatogenesis. We have carried out studies with local injections of griseofulvin suspension directly into human tissue to observe the effect of this compound on local cellular changes. To date we have seen no significant changes as regards cellular mitosis in the hair follicle or in various skin tumors. Animal tumor studies are also in progress.

Resistance and Relapse

It is too early to arrive at any conclusion as to the possibility of development of resistance to griseofulvin or relapse after treatment with this compound. Robinson [18] recently reported that resistance to griseofulvin may be developed by sensitive fungi in cultures; we have not been able to confirm these findings clinically, since repeated cultures taken from a patient in "relapse" showed the same degree of sensitivity as the pretreatment cultures. The case in point is that of a female patient with tinea corporis due to T. rubrum involving one buttock which cleared up, with negative culture, within six weeks and then presented what appeared to be a true relapse; that is, the center of the original lesion flared up, in spite of careful precautions against reinfection. The patient again was placed on therapy with orally given griseofulvin, and the cultures again became negative. Several subsequent outbreaks have been successfully controlled with topical applications of griseofulvin.

The opinion of some investigators that this type of recurrence is the result of insufficient length of therapy is difficult to accept when, after each dis-

*Results of Therapy with Orally Given Griseofulvin in Eighty-four Patients with Ringworm Disease**

Condition and Causative Organism	Patients							
		Sex						
	No.	M	F	Age, Yr.	Dosage†	Duration of Therapy	Results‡	Side-Effects
Tinea capitis								
Microsporum audouini	8	8	0	3-10	250 mg. b.i.d. or q.i.d.; 1-250 mg. t.i.d.; then 5 Gm. single dose	1-8 wk	5 cleared, 1 improving, 2 i.t.e.	Gastric discomfort (temporary) in 2
Microsporum audouini	13†	12	1	4-11	5 Gm. single dose	1 day-8 wk	2 cleared, 1 relieved, 9 i.t.e., 1 worse	None
Microsporum canis	4	4	0	3-7	250 mg. q.i.d.	4-8 wk	4 cleared	None
Trichophyton tonsurans	1	0	1	35	250-500 mg. q.i.d	1 wk.	Improving	None
Tinea corporis								
Trichophyton rubrum	22	15	7	4-56	250-500 mg. q.i.d.	1-14 wk.	3 cleared, 8 improving, 1 relieved, 10 i.t.e.	Anorexia and insomnia in 1, nausea in 1
Trichophyton gypsum mentagrophytes	7	4	3	6-44	250-500 mg. q.i.d.	1-18 wk.	1 cleared, 6 improving	Weepiness in 1
Microsporum canis	1	0	1	6	250 mg. q.i.d.	3 wk.	Cleared	None
Microsporum audouini	1	1	0	5	250 mg. q.i.d.	2 wk.	Cleared	None
Tinea cruris								
Trichophyton rubrum	2	1	1	19,37	250-500 mg. t.i.d or q.i.d.	4-10 wk.	1 cleared, 1 relapse	None
Trichophyton mentagrophytes	4	4	0	22-54	250-500 mg. q.i.d.	1-3 wk.	1 cleared, 2 improving, 1 i.t.e.	Hot flushes in 1
Tinea pedis								
Trichophyton rubrum	6	4	2	23-55	250-500 mg. q.i.d.	1 day-4 wk.	3 improving, 3 i.t.e.	Headache in 1
Trichophyton mentagrophytes	2	1	1	35,37	*250-500 mg. q.i.d.*	*1 day-2 wk.*	1 improving, 1 i.t.e.	None
Onychomycosis								
Trichophyton rubrum	13	6	7	17-50	250-500 mg. q.i.d.	2-20 wk.	4 cleared, 3 improving, 6 i.t.e.	Dizziness (temporary) in 2
Trichophyton mentagrophytes	1	0	1	35	250-500 mg. q.i.d.	2 wk.	Improving	None
Saprophytes	1	1	0	25	...	3 wk.	Improving	None

* There were 84 patients in study; table shows 86; 2 had fungous infections in 2 locations and are thus listed twice.

† *We have recently started to test feasibility of therapy with single doses of 5 Gm. of griseofulvin. Of 40 additional patients who received this* single 5-Gm. dosage for infections due to M. audouini, 23 cleared and 7 are still under observation; 2 of the 23 had to be retreated with 5 Gm. to clear. Ten patients did not return for detailed laboratory follow-up studies, and 30 showed no signs of any reactions.

‡ Cleared: microscopic slide and culture negative; lesions healed; no fluorescence of involved hair. Improving: lesions healing and cultures improving, indicating eventual eradication of infection. Relieved: early signs of improvement; e.g., disappearance of itching, better perspiration, and some regression of lesions. I.t.e.: insufficient time elapsed since start of therapy for clearing. Duration of disease in these patients varied from two weeks to 30 years. *Degree of response is apparently not affected by duration of disease.*

continuance of the drug therapy, cultures and microscopic examinations of tissue sections proved totally negative and lesions had healed completely. It appears true, however, that most so-called relapses are actually cases of reinfection, an easily understandable fact when one considers the ability of fungi to survive under almost any conditions and the presence of infected areas in other parts of the body. It also should be borne in mind that repeated relapses in patients with infections due to T. rubrum may be associated with severe systemic conditions, such as Cushing's syndrome, which are known to render the keratinous layer of the skin more vulnerable to invasion by this pathogen. Therefore, failure to control these systemic conditions may be the cause of relapses. As Burkholder[17] states, "Emergences of drug-resistant cells from a general population of drug-susceptible organisms can create serious problems." We have no information as yet with regard to the possibility of repeated reinfection after cure with griseofulvin. Also, as yet, we have no information on the course of infections induced by fungi from patients treated with griseofulvin.

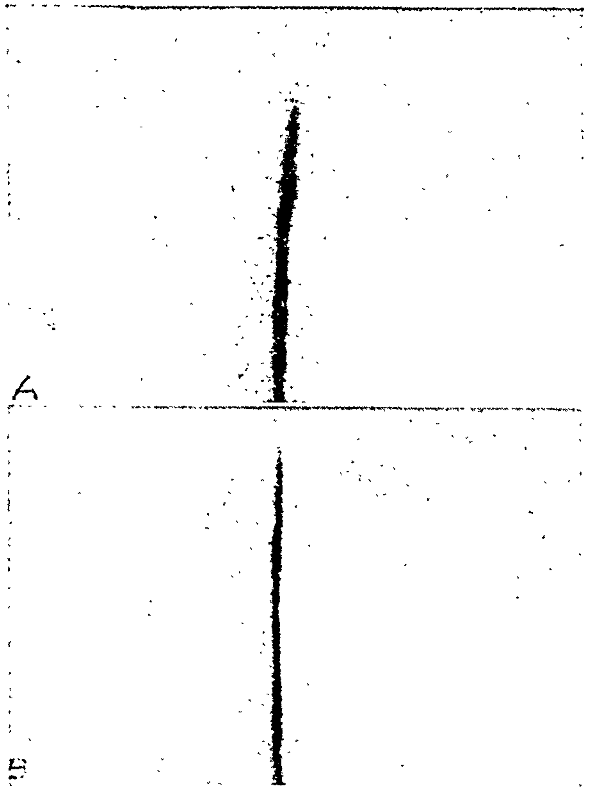

Fig. 3.—Trichophyton gypseum (mentagrophytes). Top, **infection of buttock, recurrent for more than 10 yr.** ***Bottom,*** **after one week of oral griseofulvin therapy, 2 Gm. daily.**

Therapeutic Results and Side-Effects

Orally Given Griseofulvin.—Griseofulvin was administered orally to 84 and topically to 91 patients with various types of ringworm infection. The results of this method of treatment are shown in the table.

Topically Given Griseofulvin.—The discouraging report by Grant-Peterkin[18] that griseofulvin, in spite of its high effectiveness when given orally, is relatively ineffective as a topical antifungal agent and Pardo-Castello's report[7] that topically given griseofulvin did not produce permanent fungicidal activity, presented us with a challenge to pursue further investigative studies with regard to this problem. A special griseofulvin lotion for topical application was prepared. This was an investigative material containing about 1.5% of griseofulvin suspension with surfactants, stabilizer, and urea in a glyceride oil. We used this investigative topical griseofulvin preparation on 91 patients with tinea capitis, corporis, cruris, and pedis due to T. rubrum, T. mentagrophytes, and M. audouini. Despite the relatively recent start of this study, the affected areas in a number of patients have cleared completely and many of the remainder are showing satisfactory improvement (fig. 3, 4, & 5). Because of the discouraging results (relapses and vesicular reactions) of orally given griseofulvin treatment of tinea pedis, special griseofulvin mixtures are being given topically for this condition. Eczematous dermatitis developed in one patient in this series and results of a patch test to griseofulvin were negative. Detailed laboratory and clinical studies are being

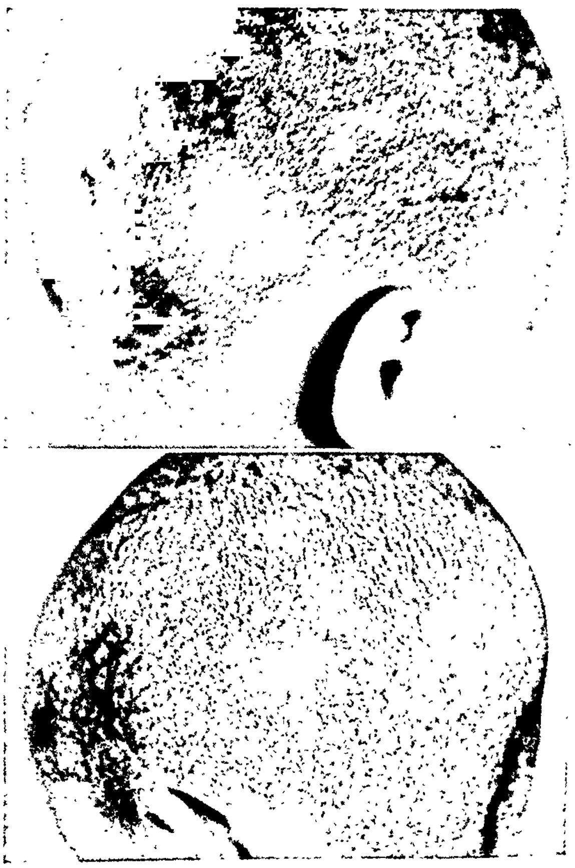

Fig. 4.—Tinea capitis. ***Top,*** **tinea capitis due to Microsporum audouini.** ***Bottom,*** **after 1 Gm. of griseofulvin per day for three weeks: cultures and results of Wood's light examination negative.**

done with several other types of topically given griseofulvin lotions to attempt to define the value of the griseofulvin itself in such mixtures.

In uncontrolled experiments a number of patients with extensive tinea versicolor also have responded, at least temporarily, to topical administration of griseofulvin; control studies are now under way on the vehicle alone. While it is too early to reach definitive conclusions, our studies seem to indicate that the problem is one of achieving good diffusion into the keratin, rather than of simple percutaneous absorption, so that griseofulvin or its metabolites become available to the fungi. The lotion produces a mild drying of the skin. This desquamative response assists the action of locally deposited griseofulvin by more effective removal of the skin in the manner in which hair growth and nail growth remove fungi in keratin. Experiments are under way with bacterium-inhibiting and yeast-inhibiting compounds added to our lotion, since bacterial and yeast infections often occur concomitantly with fungus conditions, especially in intertriginous areas and on the feet. We are also studying the feasibility of concomitant oral, lower dosage, and topical therapy with griseofulvin.

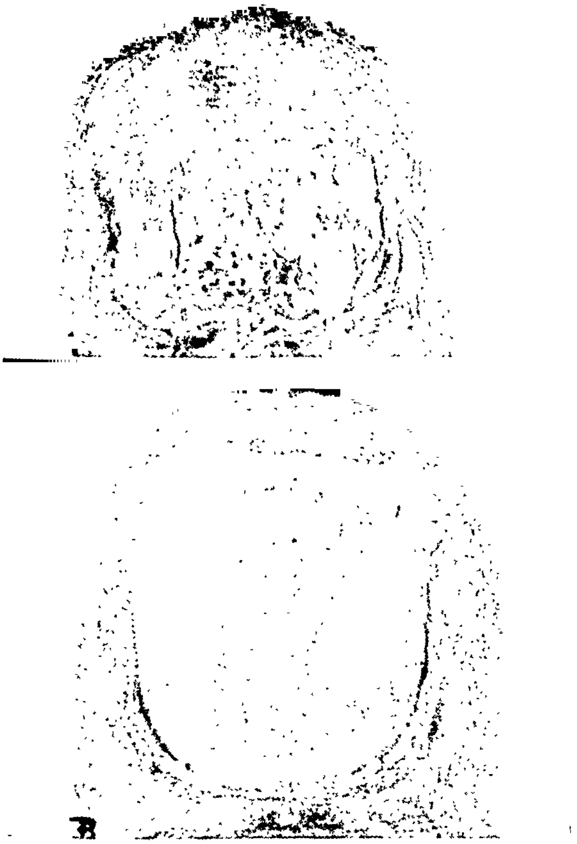

Fig. 5.—Trichophyton rubrum infection of nails, many years' duration. *Top*, therapy with griseofulvin, 1 Gm. daily, started April 23, 1959. *Bottom*, Aug. 14, 1959, cleared; culture negative.

Summary and Conclusions

Griseofulvin, a new antifungal antibiotic, was given orally to 84 patients and topically to 91 patients with a variety of ringworm infections. In adults the average oral dosage is 250 mg. three or four times daily, except in Trichophyton rubrum and Trichophyton gypseum (mentagrophytes) infections, which may require larger doses. Children generally respond to one-half of the adult dosage. Topical administration is still under study, especially in patients with tinea pedis.

Average duration of treatment varies from two to eight weeks in tinea capitis, tinea corporis, and tinea cruris; in infections located in areas of thicker skin, such as in palms and soles, somewhat longer treatment is necessary. Onychomycosis requires four to six months and even longer treatment in extensive and resistant cases and in toenail involvement.

Results are almost uniformly good, with eventual eradication of the infection, especially in tinea capitis where a complete cure may be obtained. One patient with tinea cruris due to T. rubrum relapsed each time the lesions cleared but is now under good control with topical griseofulvin therapy. Results in patients with tinea pedis are erratic. No serious side-effects were seen. Adverse reactions encountered were mild and transitory, consisting of a minimal number of cases of headache, gastric discomfort, nausea, dizziness, insomnia, anorexia, and fatigue. Patients with active peptic ulcer were given griseofulvin without untoward reactions. It is emphasized that little is known with regard to the compound's toxicity in long-term treatment. Before griseofulvin therapy is instituted, diagnosis of ringworm should be confirmed by direct microscopic examination and culture of scrapings from the involved areas, except in onychomycosis where this may be difficult to achieve. At present, this examination for fungi is best carried out by experienced medical mycology laboratories. At this time, griseofulvin appears to be an almost uniformly effective antifungal antibiotic in superficial ringworm infections, at least when given orally, and it is the treatment of choice in these conditions. There can be no doubt that this agent offers the first hope for consistent cures of these tineas.

441 Vine St. (2).

The griseofulvin used in this study was supplied as Fulvicin through Drs. Harry V. Pifer Jr. and G. Kenneth Hawkins, *Division of Clinical Research, Schering Corporation,* Bloomfield, N. J.

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DIAGNOSTIC APPROACH TO THE INFANT WITH AN ENLARGING HEAD

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Frequently, the first sign of intracranial derangement in the infant is an abnormally rapid enlargement of the head. It is usually demonstrable before disturbances of function can be detected by neurological examination. Early and definitive diagnosis is essential. The first step is routine roentgenographic study; second, investigation of the subdural space; and, third, investigation of the ventricular system and subarachnoid pathways by air contrast radiography, either ventriculography or pneumoencephalography.

Intracranial lesions in infants, resulting in damage to the cerebrum, do not usually produce clinically detectable defects in the infant's neurological function. An intracranial disorder, therefore, may progress to advanced stages of cerebral damage without being detected. Suspicion may be aroused if the infant feeds poorly, vomits frequently, is irritable, or demonstrates evidence of delayed development. If the disease process is of the space-occupying type, producing increased intracranial pressure, frequently the first indication of intracranial derangement is the recognition of abnormally rapid enlargement of the head. The clinician is then confronted with the differential diagnosis between hydrocephalus, chronic subdural collections, and brain tumor. Under these circumstances, progressive head enlargement means progressive brain damage. Consequently, early recognition; prompt, accurate diagnosis; and early treatment are mandatory before irreversible brain damage is produced.

The practitioner is conscious of the importance of head size in infants and the rate of increase. Therefore, clinical evaluation of head growth is a routine part of evaluation of the well baby. If one becomes suspicious of abnormal head growth, the head should be measured daily with a steel tape, by the same person, at the same point of widest circumference of the head, until it is definitely established that steady enlargement is occurring at an abnormal rate. In infants with acute states of increased intracranial pressure, bulging of the fontanels will be a prominent feature. However, in the presence of chronic intracranial disease the fontanels may often appear normal. As soon as it is well established that progressive enlargement is occurring at an abnormally rapid rate, specific diagnostic studies should be instituted.

The definitive diagnosis of the mechanism of abnormal head enlargement in infancy is determined by the following steps: (1) routine roentgenographic examination of the skull; (2) investigation of the

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subdural space by subdural tap; and (3) investigation of the ventricular system by contrast roentgenographic air study—either ventriculography or pneumoencephalography.

[illegible] and candling of the head are both innocuous procedures which may provide a clue to the presence of intracranial disorder, but neither study provides information of conclusive diagnostic value. If either of these studies gives negative results, it does not rule out the presence of intracranial pathology.

Studies of the elimination of dye and hydrodynamic studies without air-contrast roentgenography do not provide definitive information about the mechanics of abnormal head enlargement. The use of these studies should be avoided because the meager evidence obtained does not justify the risk of repeated needle puncture into the subarachnoid space or ventricle which is required for their performance. Repeated punctures invite infection which, especially in an infant with hydrocephalus, will compound the original disorder and often destroy any possibility of obtaining a satisfactorily functioning shunt mechanism.

Routine Roentgenographic Examination of the Skull

Routine roentgenographic examination of the skull is the first step in definitive diagnosis. The study will confirm the clinical impression of an abnormally enlarged head and may give a clue to the basic disease process present. The procedure is completely innocuous and, if the first study gives a negative result, should be repeated if clinical signs indicate progression. The first film study in this instance would serve as a basis for comparison. Enlargement of the cranial vault may be roentgenographically demonstrated by the discrepancy in the size of the vault as compared to the size of the face. This is usually associated with splitting of the sutures, particularly the coronal sutures, and perhaps the roentgenogram will show the soft tissue shadow of a bulging fontanel.

In infants with hydrocephalus, symmetrical enlargement of the skull, with thinning of the bones of the cranial vault and prominence of the frontal region may be demonstrated. In those with internal hydrocephalus, there are often present a shallow posterior fossa and split sutures, which may be suggestive of aqueduct stenosis.

The infant with chronic subdural collections has characteristic biparietal head enlargement. This is usually not associated with selective thinning of the bone, and prominence of the frontal region is not present. Roentgenograms of infants with cysts of the fourth ventricle, on the other hand, characteristically demonstrate enlargement and elongation of the posterior fossa, with a normal anterior fossa.

In a case in which there is a tumor in the posterior fossa, there may be asymmetrical thinning of the occipital bone, in addition to the other roentgenologic findings of internal hydrocephalus. When tumors of the hemisphere are present, head enlargement is often asymmetrical. Thinning of the bone may be present on the side of the lesion, and occasionally calcific deposits may be found in the body of the tumor.

Investigation of the Subdural Space

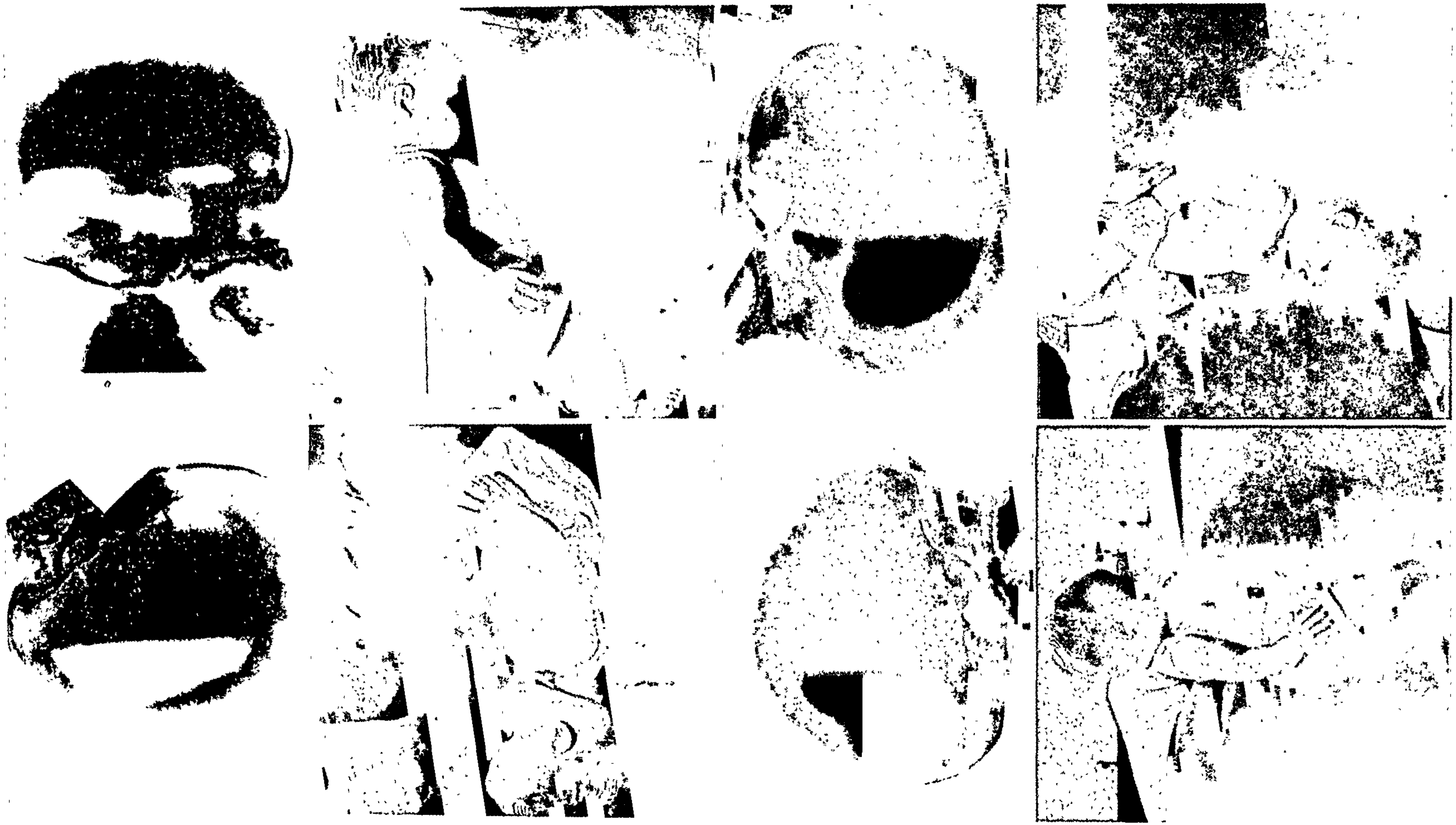
Steps 2 and 3 require needle entrances into the subdural space, ventricular system, or subarachnoid space. These procedures, in addition to inviting infection, also disturb the intracranial hydrodynamics and may precipitate an acute crisis which must be followed by definitive or palliative surgery. With the clinical data available at present, the diagnostic approach should be planned carefully, according to the tentative diagnosis, and those procedures should be used which will provide maximum information with minimum manipulation of the intracranial structures.

If bilateral subdural taps yield bloody or xanthochromic fluid, which establishes the presence of an acute or chronic collection in the subdural space, the anatomic extent of the collection may be confirmed by the injection of a few cubic centimeters of air into the subdural space and the taking of roentgenograms of the skull in various projections. Pneumoencephalography should be performed to visualize the ventricular system and the subarachnoid pathways, in order to establish the presence or absence of associated hydrocephalus or tumor.

Air Contrast Studies

If the subdural taps show normal findings, air contrast studies of the ventricular system should be performed as step 3 in the diagnostic approach, preferably at the same session.

In the presence of obvious increased intracranial pressure, and especially if a posterior fossa lesion is suspected, ventriculography is the preferred procedure. A 2.5-in. 20-gauge needle of the type used for lumbar puncture is directed slowly through the coronal suture, preferably into the potentially nondominant hemisphere, in the direction of the lateral ventricle. Note is taken of the depth at which fluid is obtained. If the pressure is markedly elevated in the ventricle, fluid is allowed to drain slowly until the pressure has been reduced to normal. Between 40 and 50 cc. of ventricular fluid is then replaced with an equal volume of air in 5-cc. increments. Total drainage of the ventricular system and the use of large quantities of air is poorly tolerated by infants and should be avoided. By proper manipulation of the head, the bubble of air can be selectively placed into every portion of the ventricular system, and the entire system can be visualized for study by means of roentgenography. The use of multiple views in such a study must be stressed. It has been advocated that this method be used in patients with clinically diagnosed hydrocephalus and that an upright anteroposterior and lateral film be taken to visualize the thickness of the cerebral cortex to determine whether shunting procedures would be advisable. If multiple views are not taken, a tumor may easily be overlooked.



Steps in manipulating air from lateral ventricle through ventricular system to visualize posterior fossa. In step 4 notice air in fourth ventricle and spinal canal, demonstrating patency of aquaeductus cerebri and of fourth ventricle.

The most important phase of the ventriculographic study is the manner in which the child is manipulated to displace intraventricular fluid and manipulate the bubble of air through the interventricular foramen into the third ventricle and through the aquaeductus cerebri and fourth ventricle into the spinal canal. This maneuver will result in visualization of these structures and demonstrate communication of the ventricular system with the spinal canal (see figure). First, the child is held face down to place the bubble of air in the posterior part of the lateral ventricle and dislodge it from the temporal horn. Second, the child is placed in the upright position. The bubble of air in this position moves to the top of the lateral ventricles. Third, the child is slowly moved backward until he is supine. The air thus moves to the anterior portion of the lateral ventricles and begins to flow through the interventricular foramen into the third ventricle. The turning maneuver is then slowly completed by inverting the child, which brings the third ventricle, aquaeductus cerebri, and fourth ventricle in a superior position and permits the air to flow into these structures. A lateral film of the skull is then exposed.

In the absence of a block, air will enter the spinal canal, demonstrating the patency of these structures. In this manner, retrograde myelography can be performed to visualize the entire spinal canal.

Stenosis of the aqueduct will be demonstrated by visualization of the dilated portion of the aqueduct above the block. This portion will be in normal position and will appear as a dilated, rounded stump of aqueduct. In the presence of a tumor in the posterior fossa, with complete or partial block, the aqueduct will be seen as a pointed structure displaced anteriorly by external compression.

In the study of an infant with a cyst of the fourth ventricle, the ventricular structures will be displaced anteriorly. Air may not be displaced into the cyst, which often does not completely block the aquaeductus cerebri.

If the posterior fossa structures cannot be clearly demonstrated by this method, then the child should be placed in the sitting position, a lumbar puncture performed, and air admitted to the subarachnoid space by the positive pressure technique, as a supplementary pneumoencephalogram to define this area more clearly.

The Role of Pneumoencephalography

Pneumoencephalography is the more precise method of study, since it visualizes the basilar cisterns and the subarachnoid spaces over the cortex as well as the ventricular system. This procedure has probably not been adequately used for the detection of intracranial disorders in infants because, in most instances, increased intracranial pressure is present at the time air study is considered and, as a result, pneumoencephalography is associated with an increased risk to the patient. For this reason, there is a widespread impression that the procedure is contraindicated at any time an expanding intracranial lesion, particularly a lesion in the posterior fossa, is suspected.

On the contrary, pneumoencephalography, performed by a well-trained operator who uses the positive pressure technique of air injection, is a safe procedure which is well tolerated by infants, provided markedly increased intracranial pressure is not present. The study should be used as a primary air study if there is no clinical indication of marked increased intracranial pressure, and it may be used as a secondary air study to supplement ventriculography for more precise visualization of the posterior fossa, the basilar cisterns, or the subarachnoid pathways over the surface of the cortex.

Pneumoencephalography in infants is a microcosm of pneumoencephalography in adults. The positive pressure technique described by Lindgren[1] and Robertson[2] is recommended. The child is placed in the sitting position and lumbar puncture is performed. Care is taken not to release fluid from the spinal canal before air is injected. The direction of flow of air into the intracranial structures can be selective and is governed by the position of the head. When the head is flexed about 40 degrees, air will flow directly into the fourth ventricle and the remainder of the ventricular system. If selective visualization of the basilar cisterns is desired, the head may be extended and, in this position, a small quantity of air will ascend directly in front of the cord and brain stem to visualize the basilar cistern and eventually fill the subarachnoid pathways over the surface of the brain. With use of this technique and with the exchange of 3 or 4 cc. of fluid at a time, excellent visualization of the ventricular system, the basilar cisterns, and the subarachnoid pathways has been obtained consistently in infants.

Summary

Intracranial disease involving the cerebrum in infants does not usually produce alteration in the infant's neurological function. The first sign of intracranial disease may be progressive abnormal enlargement of the head.

The definitive diagnosis of the mechanisms of head enlargement is obtained by (1) routine roentgenologic examination of the skull; (2) investigation of the subdural space by subdural tap; and (3) contrast air studies of the ventricular system and subarachnoid pathways, by either ventriculography or pneumoencephalography.

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DANGERS OF EXCRETORY UROGRAPHY

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The diagnostic value of excretory urography justifies its extensive use provided its limitations are recognized and its dangers are appreciated. It should not become merely a routine study, and the exposure of the patient to radiation should be limited. In a series of 21,525 intravenous urograms there have been no fatalities, but there were four serious reactions in which death was narrowly avoided. The patients were two men aged 35 and 69 years and two women aged 44 and 61 years. Three of the four required intubation and prolonged artificial respiration. Certain precautions are recommended to preclude allergies, over-sedation, and excessively rapid injections, but, in addition, it is suggested that all excretory urography be done in a surgical suite where oxygen, cut-down sets, cardiac arrest trays, and the services of an anesthetist are available.

Excretory urography has been developed to such a degree of perfection and has been so widely accepted as a diagnostic tool that, paradoxically, certain evils may have arisen in connection with it. It is invaluable and irreplaceable in certain circumstances and is undoubtedly the best method for the routine screening of the upper urinary tracts before prostatic surgery and for the postoperative check after pyeloplasty, ureteral anastomosis, or urinary diversion in a case in which the passage of a ureteral catheter is impossible or is likely to traumatize the operative site. It is also the preferred method of appraisal of the kidneys in patients with malignancies arising from the cervix, prostate, rectum, or urinary bladder. The spread of these malignancies frequently involves the lower part of the ureter, producing stasis, and catheterization in these patients should be avoided. In patients with renal stones and uninfected urine, excretory urography is preferred. If infection is introduced in such cases, it is virtually impossible to eliminate it and it usually leads to rapid progression of the disease.

Arguments Against Excretory Urography

There is often a choice between the use of excretory urography and cystoscopy with retrograde pyelography, and this paper is not intended as a diatribe against the use of excretory urography but rather as an attempt to appraise its true worth. The two methods of visualization should be regarded not as competing but rather as complementary procedures, each having its own field of usefulness with an overlapping midzone.

The method used should be decided on only after all preliminary studies have been completed and some idea of the underlying disease processes has been formed. X-ray examination is the culmination of the study, not the initial effort. Neither method should be routine and careful planning will avoid repeated exposure of patients to radiation.

The dangers of excretory urography fall into two main groups. First, the method may be used incorrectly or in patients in whom it is incapable of revealing the proper diagnosis, thus needlessly delaying treatment; second, there are dangers inherent in the intravenous injection of radiopaque substances.

Blood in the urine is an indication for cystoscopy without delay, since early malignancies in the bladder may not be visualized on excretory urography. This point was forcibly brought home to us by a patient seen recently. A 73-year-old woman had gross hematuria for six months. She was examined by excretory urography, which showed normal findings. Further investigation was delayed and only done, because of persistent severe bleeding, six weeks later, when a high-grade infiltrating cancer of the bladder was found.

With the increasing awareness of the possible significance of hematuria this kind of accident is becoming more rare, but we must caution against the natural reluctance of the pediatrician to suggest instrumentation. The history of a 27-month-old child who had hematuria for 15 months before cystoscopy was performed has already been reported by our service.[1] When cystoscopy was finally performed a fleshy tumor of the fundus of the bladder was seen, and on removal this proved to be a hemangioma. Pyuria also is often better investigated by cystoscopy and pyelography, because the opportunity can be taken to collect separate urine samples from the two kidneys and determine the origin of the pus.

In the past it has been usual to examine young patients who have hypertension by means of excretory urography. Prompt bilateral function was thought to exclude renal vascular abnormalities. We now know that this is not true, and cases have

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been reported by Poutasse and Dunstan [2] and Conner and others [3] of normal excretory urograms in patients with hypertension due to renal ischemia.

Fig. 1 is the excretory urogram of a 41-year-old man who appeared with severe headaches and hypertension. There was good bilateral function in five minutes, but ureteral catheterization with divided function studies showed that the right kidney was functioning poorly. Femoral aortography was then performed and showed a plaque at the right aorticorenal junction. This plaque was removed by Dr. S. A. Wesolowski, and the patient's blood pressure became normal. It has remained so for 12 months. Postoperative excretory urography (fig. 2) and divided function studies showed that the right kidney is now functioning normally.

What of the dangers which attend the intravenous injection of radiopaque material? Fortunately they are small. Pendergrass and others [4] reported 31 deaths in a collected series of over 3 million urograms; 25 were described as immediate and 6 as delayed. The reports of some of these deaths are horrifying. For example, a young woman received 2 ml. of iodopyracet (Diodrast) under the tongue as a test. A few minutes later 1 ml. was injected intravenously, and several minutes later the main injection was begun. After 5 ml. had been injected she complained of intense desire to urinate, had a convulsion, and died.

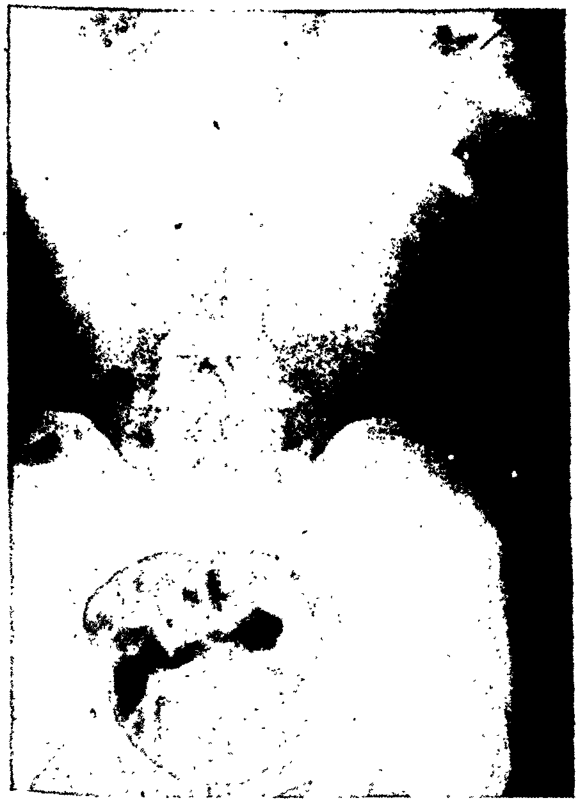

Fig. 1.—Excretory urogram (five-minute film). Note good bilateral function, although patient has atheromatous plaque at right aorticorenal junction.

Our data are from a series of 21,525 intravenous urograms, 14,173 performed at the department of roentgenology and divisions 1 and 2 of urology, Kings County Hospital, from April, 1953, through January, 1959; 4,816 performed at the division of roentgenology and urology, Brooklyn Hospital, from April, 1946, to January, 1959; and 2,546 performed at the departments of roentgenology and urology from 1949 through April, 1953. Although these injections were not actually performed by us, most of the examinations were made during the tenure of one of us (F. C. H.) as chief attending urologist.

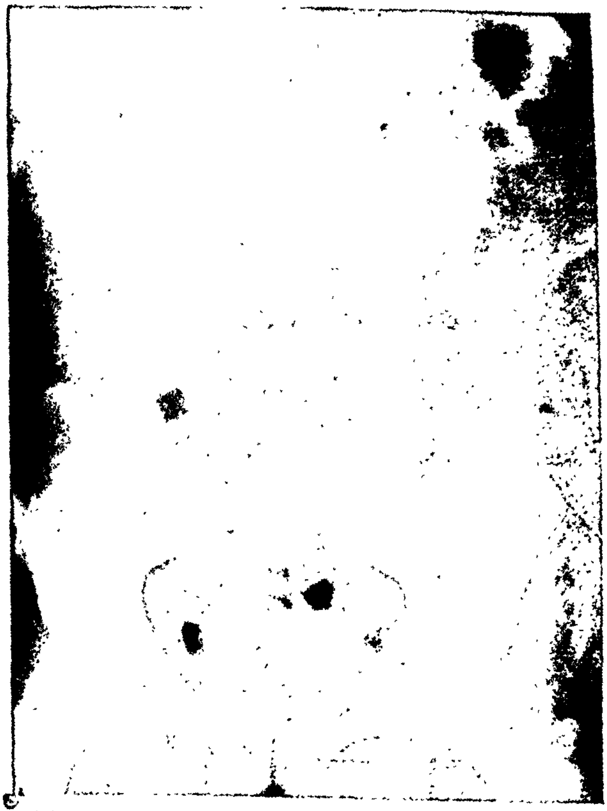

Fig. 2.—Excretory urogram (five-minute film) of same patient as in figure 1, made after removal of right aorticorenal plaque.

Although there have been no fatalities we have had four serious reactions in which death was narrowly avoided. Of the serious general reactions three occurred after the injection of 50% diatrizoate (Hypaque) sodium and one after the injection of 50% sodium iodomethamate (Neo-Iopax). Since this paper was completed there has been another serious reaction, this time to 60% methylglucamine diatrizoate (Renografin). The case histories of these patients are as follows.

Report of Cases

Case 1.—A 69-year-old man was referred for investigation of symptoms of prostatic hyperplasia. He complained of nocturnal dyspnea and precordial pain radiating to the back of the neck. He also complained of mild asthma. Electrocardiographic findings were normal.

Prior to urography he received no sedative or antihistamine medication. On Sept. 13, 1956, after intravenous injection of 3 ml. of diatrizoate, he developed a severe shock-like state. His blood pressure was unobtainable, and his pulse and respirations were rapid. An infusion was started and 0.5 ml. of 1:1,000 adrenalin given intravenously. Diphenhydramine (Benadryl) hydrochloride, 15 mg., was given intravenously. His respirations slowed and he became cyanosed. An anesthesiologist performed intubation and artificial respiration. His cardiac and respiratory status gradually improved, and an electrocardiogram taken the next day showed no abnormality. Six days later a repeat excretory urogram was taken. During the intervening period he had received diphenhydramine, 100 mg., four times daily. This time 20 ml. of 50% sodium iodomethamate was injected intravenously, and no reaction was observed.

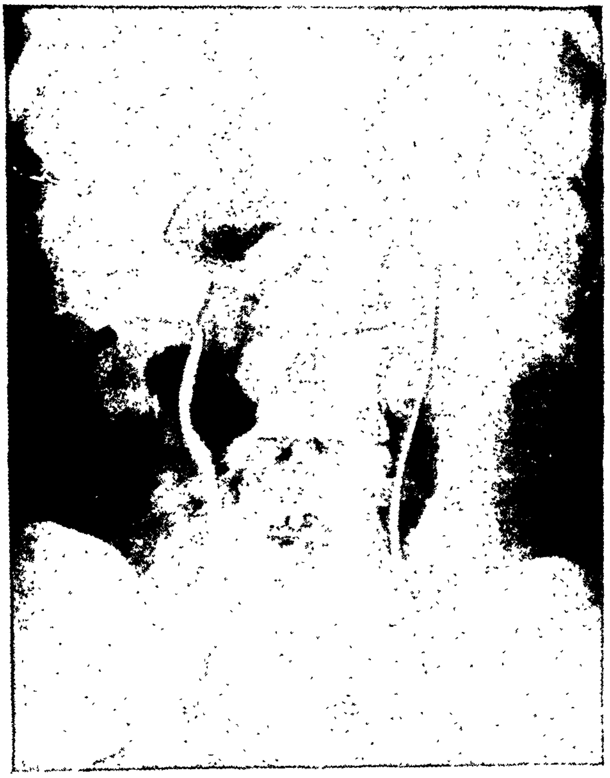

Fig. 3.—Normal-appearing retrograde pyelogram of patient with urinary tract infection.

Comment.—This patient had a history of cardiac disease and asthma. We believe that this combination is a contraindication to excretory urography. The other point of interest is that when excretory urography was performed for the second time no reaction occurred. This may be attributed to either the antihistamine medication or to the change from diatrizoate to sodium iodomethamate. Even though this patient did not suffer a reaction we believe that this second procedure was unwise, notwithstanding the change of medium.

Case 2.—A 35-year-old man was referred as an outpatient for excretory urography because of symptoms of dysuria and frequency. He had no history of cardiac disease, and his electrocardiogram was normal. No medicaments were given preoperatively. On Oct. 2, 1956, 20 ml. of diatrizoate was given intravenously, and he complained of no untoward symptoms for 30 minutes. It was not until he arose and started to dress that he collapsed. No blood pressure reading could be obtained, and his pulse was rapid and irregular. He was given oxygen, and an infusion was started; 100 mg. of chlorpheniramine (Chlor-Trimeton) maleate and 0.5 mg. of adrenalin were given intravenously. Continuous infusion of phenylephrine (Neo-Synephrine) hydrochloride for six hours was required before the patient's blood pressure stabilized at 100/80 mm. Hg; 12 hours after the reaction his pulse was still irregular, and his electrocardiogram showed auricular fibrillation. Thirty-six hours after the reaction the sinus rhythm suddenly reverted to normal and the patient was discharged on Oct. 4, 1956.

Comment.—This is an example of a delayed reaction, as described by Pendergrass. The patient seemed in perfectly satisfactory condition until 30 minutes after injection of the contrast medium.

Case 3.—A 61-year-old woman, an outpatient, who had no premedication, received 1 ml. of diatrizoate, and after three minutes another 10 ml. of the medium was given slowly, on Jan. 7, 1957. She vomited and became pale. She then became confused, she breathed rapidly, and a blood pressure reading was unobtainable. The department of anesthesia was notified, and no time was lost in performing a cut-down, since it was impossible to introduce a needle into one of her veins because of shock and obesity. She was given oxygen by mask, intubated, and given artificial respiration. Phenylephrine and levarterenol (Levophed) bitartrate were required to maintain her blood pressure. This patient made a complete recovery.

Comment.—Inquiry after her recovery from the reaction revealed that this patient had a history of strong allergy. If we had been aware of this, urography would not have been performed.

Case 4.—An excretory urogram was advised in a 44-year-old woman because of a history of recurrent pyuria, dysuria, and frequency. She had a moderate degree of cardiac decompensation and complained of shortness of breath on exertion. On June 25, 1958, 1 ml. of 50% sodium iodomethamate was given intravenously, followed in three minutes by the injection of 20 ml. Nothing untoward was observed, and the physician left the room for about 10 minutes. During this interval the nurse noted that the patient was breathing heavily and developed marked swelling of the face and lips. Her labored breathing suggested constriction of the trachea. The department of anesthesia was informed, and in the meantime oxygen was given nasally. An infusion was started because the blood pressure could not be obtained. Chlorpheniramine was given intramuscularly. The anesthetist intubated the patient. Artificial respiration was necessary for 15 minutes. An electrocardiogram showed probable old myocardial infarction. Recovery was slow, but she was able to be up 24 hours later.

Comment.—In two of our patients epinephrine was given intravenously. One of these cases has been reported in detail,[5] and in that paper the comment was made that the administration of epinephrine intravenously in these patients is unwise.

Treatment of these patients should fall into three phases: (1) establishment of an adequate airway, with oxygen and artificial respiration if required: (2) support of blood pressure by intravenous infusion with 5% glucose, phenylephrine, or levarterenol added as required; and (3) intravenous injection of an antihistamine.

Comment

These four serious reactions, which required specialized help in order to prevent fatalities, have convinced us that excretory urography should only be done under conditions which facilitate the prompt and vigorous resuscitation of a collapsed patient. We now do all excretory urography in a surgical suite where oxygen, cut-down sets, cardiac arrest trays, and the services of an anesthetist are available. Three of our four patients required intubation and prolonged artificial respiration.

Because of our two experiences with delayed reactions and the three reported by Pendergrass and co-workers we have now increased the time between the test dose and the definitive injection; 1 ml. is given intravenously and the patient is observed closely for 30 minutes. We are not convinced of the value of this test but we use it because other tests such as intraocular and subcutaneous injections have proved completely unreliable.

Sedation of the patient prior to the investigation is helpful in relieving apprehension and limiting air swallowing, but in elderly patients we strictly limit the dose. Oversedation causes some degree of hypoxia and increases the irritability of the heart. Most of our patients now receive a moderate dose of promethazine (Phenergan) hydrochloride the night before the procedure and again before cystoscopy.

We use a slow injection of radiopaque medium because Lyons [6] has shown that when a large bolus is injected rapidly, as in angiocardiography, there are marked changes in the electrocardiogram. We have made electrocardiograms in our patients during and immediately after the injection of contrast material given slowly. Even in these patients there were minor changes in the electrocardiogram, and in one patient who had ischemia the degree of ischemia was seen to increase.

We do not perform excretory urography on patients who have a history of asthma or allergy, nor do we use the technique of double dosage in patients whose kidneys are poorly visualized because of early renal failure. Intravenous injection of contrast material is of course entirely contraindicated in patients with established renal failure and nitrogen retention.

Urography which is performed with the patient in the supine position only may give incomplete information. Fig. 3 is the pyelogram of a 31-year-old woman who had recurrent bouts of urinary tract infection. It was not until urograms were made with the patient sitting up (fig. 4) that the diagnosis was made.

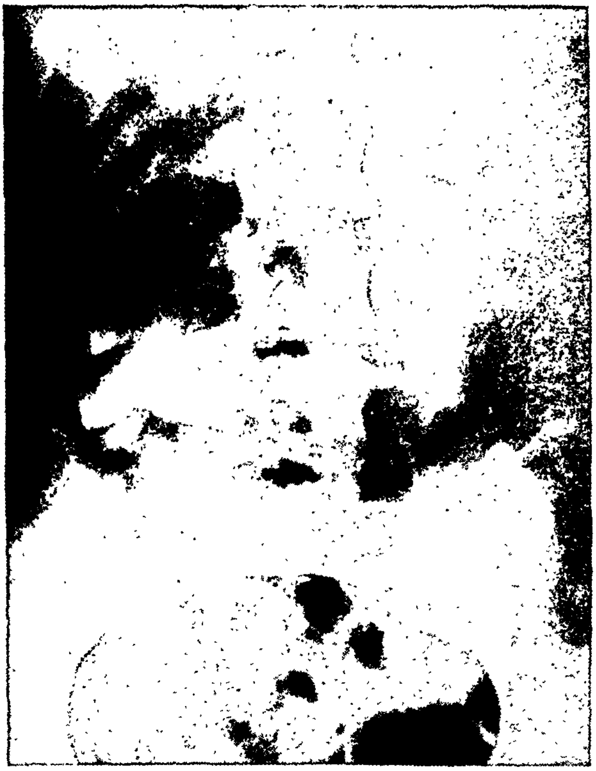

Fig. 4.—Excretory urogram of same patient as in figure 3, made with patient in erect position. Note hydronephrosis on right.

In an attempt to limit the exposure of the patient to radiation we reduce the number of films as much as possible. In many cases only a plain film and one film with contrast medium are required. Because of this all films are viewed by a physician as they are made, and a serious effort is made to prevent urography from becoming merely a routine study.

Conclusions

The dangers arising from the use of excretory urography are principally (1) overextension of the use of this highly developed modality and (2) the possibility that it will be used in patients in whom it is incapable of revealing the diagnosis, for example, those with early operable lesions of the kidney and those with small bladder tumors. Also, in the study of patients with hypertension a normal urogram does not rule out the kidneys as a possible cause.

Every precaution must be taken to prevent reactions occurring after the administration of the radiopaque medium; severe allergies and asthma are contraindications to excretory urography. The use of antihistamines as a preventive measure is being continued, but there is not enough evidence to believe that they will eliminate severe reactions. An elaborate surgical set-up should be readily available.

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CURRENT CONCEPTS OF PNEUMOCONIOSIS

PATHOLOGICAL ASPECTS

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The clearance of dust particles from the pulmonary alveoli toward the bronchi depends to some extent on adequate respiratory excursions of alveolar walls. Dust particles not so removed can penetrate the alveolar membrane instead; it is now believed that naked dust particles can pass directly through the alveolar membrane and are not carried by macrophages. In silicosis the silica-bearing cells in the characteristic nodules are thought to be proliferated alveolar cells that have remained in situ instead of desquamating. In explaining the subsequent fibrosis it is now postulated that silica crystals possess surface activity which denatures proteins and that the deposition of beta and gamma globulins in the nodules is indicative of a subsequent immune reaction. Tuberculosilicosis must be considered as a special case of a general disease process for which the more inclusive term "tuberculopneumoconiosis" is proposed.

When theory is confused with fact, the process of questioning and testing is discouraged and progress is arrested. Recognition that our present concept of pneumoconiosis rests on certain suppositions rather than on facts should cause a shift from complacent acceptance to critical inquiry.

For example, the current concept of pneumoconiosis is based on the assumption that dust-filled alveolar macrophages (1) "electively" migrate to bronchiolar ciliated epithelium, (2) "electively" penetrate the respiratory membrane, (3) "electively" migrate toward lymphatic vessels, and (4) "electively" penetrate lymphatic vessel walls.

Random movement on the part of phagocytic cells is readily demonstrable in vitro. It may also be shown that certain phagocytic cells may be attracted by some particulates and repelled by others through what is recognized as positive or negative chemotropism, as the case may be. To that extent, these cells may be considered to migrate electively. There are, of course, other kinds of tropism such as photic, electric, and thermal tropism. However, the biological behavior by which the above elective migrations are assumed to take place cannot be classified under any known mechanism or tropism, nor can it be given a rational explanation.

From the Industrial Hygiene Foundation.

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Established Concept of Pneumoconiosis and Need for Additional Information

Simply stated, according to the established concept, dust particles impinging on the alveolar surface are engulfed by the alveolar macrophages, most of which subsequently electively migrate toward the ciliated bronchiolar epithelium. The cells then are transported by ciliary action toward the pharynx. Those of the dust-filled macrophages that remain in the air spaces penetrate the respiratory membrane to enter the interstitial tissue. There they travel toward lymphatic vessels but may be trapped en route in (1) preexisting lymphoid tissue and (2) perivascular or peribronchial "lymph spaces," thereby forming dust deposits. On the other hand, the dust-filled cells may find a lymphatic vessel and penetrate the wall in such large numbers that the lumen becomes permanently blocked by their bulk, thereby forming a dust depot at still another site. Other dust cells manage to find and enter a lymphatic vessel without obstructing it and then are transported by the lymphatic flow to the lymph nodes, where other dust depots are formed. In the case of quartz dust deposits, fibrosis subsequently occurs.

Any concept of pneumoconiosis must be composed of a number of interconnected mechanisms or processes, most of them quite complex. Because relatively little is known regarding these processes, much of this knowledge is conjectural or hypothetical. It is the purpose of this presentation to discuss the newer aspects of these mechanisms. The mechanisms of pneumoconiosis which are included are (1) alveolar clearance, (2) the penetration of the alveolar membrane by dust particles, (3) the development of intrapulmonary dust depots, (4) the mobility of intrapulmonary dust depots, (5) the development of nodular or diffuse pulmonary fibrosis, (6) the development of emphysema, and (7) the development of "tuberculo-pneumoconiosis."

Alveolar Clearance

According to the established concept, alveoli are kept clean by virtue of elective migration of macrophages either toward bronchioles or into the interstitium of the lung. But, as pointed out earlier, such elective cellular migration is inconsistent with present views of cellular behavior.

A few years ago a theory was proposed whereby the mechanism of the transport of dust and phagocytic cells from alveoli toward bronchi was considered to be a passive one.[1] According to this theory, the mechanism of this transport depends on adequate respiratory excursions. Since alveoli that are attached to rigid structures are limited in their ability to expand and contract, this theory would explain the alveolar stasis commonly found in regions of scars, bronchi, vessels, tubercles, and silicotic nodules as well as the pigmentation on the periphery of such structures. Recent work by Klosterkötter[2] seems to confirm that adequate respiratory excursions play an important role in the clearance of dust from alveoli. However, more data are needed to clarify the mechanism of alveolar clearance.

Penetration of Alveolar Membrane by Dust Particles

The established concept assumes that dust particles may penetrate the alveolar membrane only by being carried across this barrier through the medium of macrophages. On the other hand, Cecil K. Drinker presented evidence favoring the direct penetration of the alveolar membrane by naked particles. Nevertheless, Drinker also believed in the cellular transport of the dust into the interstitium. By means of a more artificial experimental setup, Gross and Westrick obtained results which also led to the conclusion that naked dust particles were capable of penetrating the alveolar membrane. Significant factors in this mechanism were thought to be the intra-alveolar fluctuating respiratory pressures and the alveolar respiratory excursions. Additional support for the thesis of the direct penetration of dust particles was furnished by the experiments of Hayek. This noted anatomist found that certain drugs as well as an excess of carbon dioxide may cause alveolar cells to retract their processes, become rounded, and thereby leave portions of the alveolar membrane unprotected. Thus, the penetration of naked dust particles into the lung interstitium is believed to be facilitated.

Development of Intrapulmonary Dust Depots

The accepted view pictures the development of intrapulmonary dust depots as aggregations of dust-filled macrophages in three locations: (1) perivascular spaces, (2) preexisting lymphoid tissue, and (3) obstructed lymph vessels. These macrophages are considered to have reached their respective positions by elective migration.

Recent investigations have shown that silicotic nodules consist of cell collections which are not situated within perivascular spaces as commonly believed but rather within the alveolar spaces that surround the vessels. As a matter of fact, it has been demonstrated that perivascular spaces in the lung do not normally exist and that they develop only as a result of edema.[3] According to these investigations, the silica-bearing cells which constitute the early silicotic nodules are believed to be proliferated alveolar cells that have remained coherent and also have remained attached to the alveolar wall instead of desquamating. A similar concept had previously been formulated by Hulse[4] in regard to the formation of anthracotic plaques.

Mobility of Intrapulmonary Dust Deposits

Except for several sporadic references, little attention has been given to the permanence (or the lack thereof) of intrapulmonary dust deposits. It is conceivable that a fibrogenic dust-like silica, unless permanently sequestered from the normal lung tissue, may, if mobilized, begin its fibrogenic activity at a new site of lodgment. Recent studies[5] indicate that such mobilization actually occurs and that the mobilizing force is the flow of edema fluid. Evidence[5] also has been put forward to indicate that the progressiveness of silicosis may be attributed to the recycling of the silicotic process by silica particles liberated during the mobilization. Additional support for the concept of dust mobilization recently has been given by the work of Heppleston.[6]

Development of Nodular and Diffuse Pulmonary Fibrosis

A discussion of this aspect of pneumoconiosis may conveniently consist of two parts: (1) the mechanism of fibrosis in general, and (2) the anatomic distribution of the fibrosis.

Mechanism of Fibrosis.—The mechanism of fibrosis in pneumoconiosis has been subject to much speculation, but mainly in regard to silicosis and, to a lesser degree, to asbestosis. There is little need to do more than mention the various theories which have been considered as the explanation for the development of silicotic fibrosis. The first was a mechanical theory which postulated mechanical injury to tissue by virtue of the sharp, spiculated silica crystals. Another theory postulated the generation of irritating piezoelectricity by quartz crystals embedded in tissue. A more recent theory that has been all but abandoned is the solubility theory. This theory assumed that, when silica dissolves in tissue fluid, the silicic acid so formed is toxic and fibrogenic. The theory which currently is receiving much attention postulates that silica crystals possess surface activity which denatures proteins which are coming in contact with the crystals. Some interesting and important work done in Italy[7] indicates that one significant component of silicotic nodules consists of beta and gamma globulins and suggests that an antigen-antibody reaction may be basic to the mechanism of this fibrosis.

Anatomic Distribution.—The anatomic distribution of pulmonary fibrosis in silicosis was studied by Gardner, who believed that the difference between nodular and diffuse fibrosis could be explained on the basis of adequate lymphatic drainage in the former and lymphatic obstruction in the latter. This concept has recently been criticized.[8] It would seem preferable to assume that no satisfactory explanation exists at present for the different types of pulmonary fibrosis encountered in silicosis. In experimental silicosis, diffuse alveolar fibrosis usually is associated with severe diffuse alveolar stasis, particularly of lipidic debris which often is heavily laden with silica.

Development of Emphysema

At one time, a dust was considered inert, and therefore harmless, if it was unable to stimulate the production of significant amounts of fibrous tissue in the lung substance. The work of the pneumoconiosis research unit at Cardiff[9] changed this attitude with the demonstration that soft coal dust may cause severe obstructive emphysema. Such cases with emphysema often terminated with a decompensated cor pulmonale. Since relatively heavy deposits of "inert" soft coal dust may cause this debilitating lesion, it is conceivable that other nonfibrogenic and so-called inert dusts (likewise in the form of "heavy" intrapulmonary deposits) may produce similar lesions.

Although the development of emphysema in asbestosis and silicosis has been recognized much longer, the mechanism of this emphysema is not clear. The abundance of fibrous tissue produced in these pneumoconioses could be a factor. Or are there more subtle changes of degenerative character in the noncollagenized parenchyma?

Development of Concept of "Tuberculopneumoconiosis"

The recognition of silicotuberculosis is nearly as old as that of silicosis itself. Although a progressive, massive fibrosis of the lungs discovered in British coal workers long had been considered an "infective" pneumoconiosis, it was only a few years ago that good clinical and pathological investigative work on the part of the Cardiff group of workers[10] and the excellent, painstaking experimental work in King's laboratory[11] brought about the recognition of progressive, massive fibrosis (P.M.F.) as a "tuberculoanthracosis." Experimental work recently completed in the United States indicates that, under certain experimental conditions, other inert dusts such as kaolin, aluminum oxide, and even silicon carbide also are capable of causing a massive pulmonary fibrosis in association with a tuberculosis infection.[12] Thus, the use of the generic term, "tuberculopneumoconiosis" is justified. The mechanism by which dust and infection combine to produce a disease which is not only different from that produced by either factor alone, but also more severe, requires clarification.

Summary

Recently discovered experimental evidence, furnished by leading research laboratories abroad and in the United States, sheds new light on and permits more up-to-date discussion of the various mechanisms which are necessary components of any broad concept of pneumoconiosis. One such component here suggested is termed "tuberculopneumoconiosis." More information is needed on each of the seven mechanisms discussed.

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FATALITIES IN ANESTHESIA AND SURGERY

FUNDAMENTAL CONSIDERATIONS

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The lack of uniformity in the compilation of operating room statistics makes it difficult to appraise complications and deaths occurring in patients who undergo anesthetic and surgical procedures; this has stimulated a study of the fundamentals involved. An analysis of operative mortality necessitates the identification of lethal hazards imposed on the patient, such as errors of diagnosis, errors of judgment, and errors of technique. Other factors that must be distinguished in classifying a death which occurs during or shortly after an operation are the respective etiological relationships of the anesthesia, the surgical procedure performed, the general health status of the patient, and the nature of his illness. Organizing clinical anesthesia conference programs with associated county and state study commissions is suggested as the best way to manage the total problem.

Numerous reports of cardiac arrest in recent years leave the impression that fatalities from the conduct of anesthesia and surgery are on the increase. However, the lack of definition and terminology specific to operating room deaths and the lack of uniformity in the compilation of operating room statistics preclude an accurate assay of the problem.

In May, 1958, in an attempt to rectify this situation, a resolution was prepared, requesting that the Council on Medical Education of the American Medical Association develop a classification of and terminology for operating room deaths. This was approved by the House of Delegates of the Medical Society of the State of New York.[1] In turn, this was introduced to the A. M. A. House of Delegates at the San Francisco Annual Meeting, June 7, 1958 (resolution 28).[2] On the recommendation of the House of Delegates an ad hoc committee was appointed by the Board of Trustees of the A. M. A., under the chairmanship of Dr. Huberta Livingstone, to study the entire matter. In addition, such a study would include deaths occurring elsewhere in the hospital due directly to anesthesia or to any operative procedure.

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It is to be emphasized that any study of this subject should be on a strictly factual basis. In a sense, it must be an objective, cold, statistical analysis, an attempt to establish a classified causal relationship; it is not intended to establish or determine culpability or responsibility, and any question of this should be omitted from all discussion. It is entirely a medical matter and not a legal one.

Establishment of Death

Death may be defined as the cessation of integrated life functions.[3] Life depends on the integration of the following physiological functions: ingestion, digestion, absorption, respiration, circulation, coordination (nervous system and endocrines), metabolism, excretion, and elimination. Death occurs if any of these functions is much impaired or arrested. One may distinguish between clinical death and biological death. In clinical death, essential or vital functions may be arrested and the subject be without apparent life. This is at times reversible, as when acute cardiocirculatory collapse occurs. On the other hand, biological death exists when no amount of resuscitative therapy has the potential to restore a patient to even a vegetative existence.

When death is due to impairment of the first or last three of the listed life functions, a long period of symptoms usually precedes the terminal event. Thus, chronically ill patients with prolonged intestinal obstruction or peritonitis may have passed the stage of reversibility and hence may die as a consequence of their disease and not of anesthesia and surgery. On the other hand, disturbance of the middle three functions generally precipitates the so-called sudden deaths. These are basically concerned with acute deprivation of oxygen to tissues.

In the operating room organic causes of death are secondary. They may contribute, to the extent that they distort physiological function. One must recognize, thus, that physiological mechanisms often kill without positive findings and that in many instances there are no demonstrable findings at autopsy.

Causes of Operating Room Deaths

In analyzing the cause of death in the operating room or elsewhere in the hospital one must have two objectives in mind: first, to list the sequence of operative events preceding death and establish the order of significance and, second, to list in the order of significance the role each pathophysiological entity played in shortening the life of the patient.

Analysis of operative mortality requires that, exclusive of the intrinsic disease, one must identify the lethal hazards imposed on a patient. These are best considered as being human errors in anesthesia or in surgery. Such are (1) errors in diagnosis, (2) errors in judgment, or (3) errors in technique.

Deaths in the operating room may be produced by three major stresses and, therefore, three major categories may be used for classification. Each category is distinct and specific as a cause of death. Combinations of the basic factors may exist in a given case, but one usually predominates. The predominant groups of causal factors are (1) related to anesthesia; (2) due to surgical factors; and (3) due to the patient's original disease.

Anesthetic deaths are those associated with anesthetic management and anesthetic agents. They include (1) deaths caused by overdose of anesthetic agents, (2) deaths during induction, (3) deaths caused by massive vomiting and aspiration, and (4) deaths from errors in technical management.

Surgical deaths are related to basic errors and specifically diagnostic errors, both preoperative and peroperative, and to stresses. Stresses imposed by surgery include the following causes of death: sudden overwhelming hemorrhage, continuous prolonged bleeding, wear and tear of trauma from prolonged surgery, and reflex stresses.

The physical condition of the patient (disease of patient) may lead to operating room death, especially in patients whose condition precludes tolerance to minimal surgical stress or minimal anesthetic stress and in moribund patients with general debility. Obstetric or medical lesions of critical severity which, although recognized and under treatment, may continue their lethal progression during anesthesia and accidental or incidental mechanisms which are rare, unsuspected, or obscure may also contribute to operating room death.

One should always be alert to natural causes of death during surgery. These are distinct from the disease which requires operation. In any event, every factor must be assessed as to its contribution in shortening the life of the patient. It is evident that in the operating room anesthesia and surgery are inseparable. Anesthesia is necessary; it profoundly modifies the integrative action of the nervous system, but this is usually a reversible phenomenon. By modifying the response of the nervous system to the trauma and stress of surgery, anesthesia protects the total organism.

In some instances either anesthesia or surgery may be the major contributing element responsible for the fatal result. In many instances both anesthesia and surgical factors may share important roles in causing the patient's death. To this end a further breakdown of operating room deaths is necessary, as follows[4]: (1) anesthesia sole factor; (2) surgery sole factor; (3) anesthesia major factor—surgery minor factor; (4) anesthesia minor factor—surgery major factor; (5) patient's disease major factor; and (6) indeterminate.

Deaths Associated with Anesthesia

Deaths directly associated with anesthesia should be recognized and identified. It is not sufficient to make anesthesia a catch-all for surgical deaths.

There are positive features which define an anesthetic hazard and which indicate that it is lethal in given circumstances. As with other categories there are human errors related to diagnosis, judgment, and technique.

The circumstances under which it is reasonably certain that death is related to anesthetic management are summarized as follows[5]: (1) death during induction; (2) explosion; (3) pulmonary aspiration; (4) failure to secure airway; (5) hypoxia; (6) overdose of agent; (7) technical mismanagement; and (8) maladministration of fluids (embolism). It is of paramount importance to recognize that agents per se are rarely at fault. It is the administration, the choice, or the dose which usually plays the lethal role.

Under the circumstance of "death during induction," the establishment of anesthesia as a cause is presumptive. Death may be directly attributable to anesthesia if there is no pathological cause determined. It is certainly not surgical. If a medical cause of death exists, or an acute organic catastrophe has occurred, then anesthesia could be a contributing factor but not the direct cause. (Psychological mechanisms are not considered.)

Anesthesia Personnel.—Not only the skill and training of the anesthesiologist are essential in the avoidance of anesthetic deaths but also his conscientiousness. In addition, another personal factor must be recognized, namely, anesthetist fatigue. It should be appreciated that physicians in the active clinical practice of anesthesia are usually exposed to an unvarying daily schedule which is denoted in large measure by a monotonous repitition of the same technical acts in the same environment of an operating room. This may begin at 7 a. m. and continue through the late afternoon. Time for breaks is limited, especially when the staff is short-handed. It is also likely that one man may be on call throughout the night and be up part of the night only to face another day of a regular full schedule. All these features and many more lead to operating room hypnosis. Any lack of alertness unquestionably leads to a higher rate of complications or substandard anesthesia.

At least two recommendations are evident. First, a definite midday break is necessary, "just to get out of the operating rooms," and, second, a man who has been on call the previous night should have at least the succeeding half-day free. What role the minute concentrations of anesthetic drugs inhaled or absorbed by anesthesiologists play is as yet undetermined.

Incidence of Anesthetic Deaths.—The determinants of an operating room death are limitless and entwined with local conditions. One need merely note the type of patient undergoing surgery in some institutions; the venturesomeness of the surgical team; the importance of the type of surgical procedure, i. e., intrathoracic versus peripheral surgery or intracranial versus orthopedic surgery; and the time characteristic of surgery, i. e., the rapid, expeditious surgery taught in some clinics versus the meticulous, time-consuming surgery practiced in others.

Nevertheless, the over-all operating room mortality can be placed at 1 in 1,000 to 1 in 2,000 operations. If one reviews the available statistical reports[4] one may further conclude that about one-third of the deaths may arbitrarily be attributed to anesthesia. Thus, a rough incidence of anesthesia-related deaths is 1 in 3,000 to 5,000 anesthesias. On the other hand, factors other than anesthesia account for two-thirds of the operating room deaths.

Recommendations.—Resulting from a study of present statistics the following principles and lessons can be derived[4]: 1. No "last resort" surgery should be performed. 2. Operations of necessity should be performed if the patient is not in extremis. 3. Surgery should be carefully but expeditiously performed. Even in elective surgery, in good risk patients, mortality rises more quickly after the first six to eight hours in adults. In infants and in geriatric patients the mortality advances quickly after the first four hours of surgery. Surgeons cannot operate indefinitely, regardless of the excellence of the anesthesia, and expect to have a low morbidity or mortality. 4. The greater the operative risk the greater the need for a skillful and experienced surgical and anesthetic team. In a teaching clinic this team should perform and teach, by example and not by direction, from the side lines. 5. The greater the operative risk the shorter the time the patient should be subjected to the trauma of surgery and the depression of anesthesia. The quantity of both surgery and anesthesia should be proportionally reduced. 6. All unnecessary delays should be eliminated in preparing the patient for surgery. 7. The skill and the number of personnel trained in the care of unconscious patients should be improved.

Deaths Related to Patient Disease

Deaths immediately related to the patient's disease may be classified as follows: deaths related to the disease for which operation is required; deaths due to associated constitutional (medical) diseases; and deaths of a fortuitous nature but arising from causes originating in the patient.

Thus, certain surgical conditions are conducive to moribundity and inevitable death at the present time; one example is that of severe generalized peritonitis. Furthermore, a patient may have underlying intrinsic heart disease and may suffer a coronary occlusion or have a progressive myocardial failure. Last, unanticipated catastrophes such as pulmonary embolism or cerebral accident may occur.

Case Study Conferences

The Clinical Anesthesia Conference offers the most instructive method for the analysis of anesthetic and operating room complications and deaths. It has been actively developed by the anesthesia study committee of the New York State Society of Anesthesiologists, and their cases are published in the *New York State Journal of Medicine.* The conference is patterned after the Clinical Pathological Conference, in which case histories are presented and pertinent data noted in a challenging manner. Staff discussion ensues, differential diagnostic situations are presented, and a final diagnosis is made. After the actual outcome is determined, clinical conclusions are reached. This conference can be logically developed by anesthesiologists and should be at any organizational level that will fulfill an educational need. Throughout the conference the importance of medicine in its broad aspects is applied to the patient under anesthesia. Emphasis is on the practice of medicine in the operating room and not on the technical features of anesthesia. Unusual mechanisms producing complications and fatalities are selected.

The special purpose of this conference group of reports is to analyze abnormal physiological changes and signs exhibited by patients during surgery and to diagnose the medical conditions represented. Many of these are medical problems met by the internist. The anesthesiologist, in his role of internist in the operating room unit, must diagnose these same pathological states and distinguish them from other attendant conditions related more specifically to anesthesia or surgery. For example, such problems as diabetic acidosis, insulin hypoglycemia, status asthmaticus, coronary occlusion, pulmonary edema, cardiac failure, pneumothorax, and atelectasis must be differentiated from the toxic effects of anesthetics, shock, hypoxia, and respiratory acidosis. Prompt and precise diagnosis is necessary for proper treatment. Delayed diagnosis or treatment may result in death.

The tragedy of death during anesthesia focuses attention on the second special purpose of these conferences, namely, to assess the mechanisms and causes of death during anesthesia administered by expert anesthesiologists who use methods that conform to standards generally accepted in any community. The conference therefore, intends to accomplish two purposes: (1) to emphasize the vital importance of the clinical practice of "operating room medicine" by the anesthesiologist, and (2) to focus attention on the problems in anesthesiology practice which continue to contribute to death during anesthesia even in expert hands.

Accidental and Incidental Causes of Death During Anesthesia.—The medical causes of death deserve separate attention because their importance is increasing, in view of the frequency of medicolegal and professional criticism. Such criticism is often based on the too ready assumption that every death occurring under anesthesia is caused by anesthesia or the anesthetist, in the absence of an obvious catastrophic event such as uncontrollable hemorrhage. Furthermore, these difficult diagnostic problems have been largely disregarded or slighted by investigators of death under anesthesia in spite of the prudence of having such findings recorded and remembered, especially by anesthesiologists. Awareness of these possibilities serves as an incentive to obtain an autopsy or, at least, a postmortem x-ray of the chest or spine or a postmortem puncture of the subarachnoid, peritoneal, or thoracic spaces, as circumstances warrant and permit.

The accidental or incidental causes of death under anesthesia which have come to the attention of the anesthesia study committee are as follows[6]: 1. Fracture of a cervical vertebra with compression of the spinal cord in an infant under anesthesia for repair of cleft palate. The neck was excessively hyperextended by the surgeon in order to have the infant's head rest in the operator's lap. The fracture was revealed by a postmortem x-ray examination ordered by the anesthesiologist. 2. Acute adrenal insufficiency. Abrupt respiratory and circulatory failure occurred in a middle-aged woman under an initial small dose of dilute thiopental sodium given intravenously. The intended laparotomy was never started. Autopsy showed complete replacement of both adrenal glands by metastatic carcinoma. 3. Acute hypertensive crisis and pulmonary edema due to pheochromocytoma. With the patient under general anesthesia an unknown "renal mass" was repeatedly palpated by several observers before operation, initiating a rapidly fatal chain of events. 4. Pulmonary embolus arising from thrombosed pelvic or femoral veins during unrelated procedures. 5. Spontaneous pneumothorax during pelvic laparotomy. 6. Massive pulmonary atelectasis during spinal anesthesia for subtotal gastrectomy. 7. Myocardial infarction during an entirely normal general anesthesia for colporrhaphy. 8. Air embolism during vaginal and cesarean deliveries. 9. Amniotic fluid embolism during delivery. 10. Fat embolism during surgical trauma to fat-containing tissues. 11. Intracranial hemorrhage during a normal anesthetic course for minor surgery.

Thymic Death: No case of lymphatism (status thymicolymphaticus) has been found. This once popular explanation for death under anesthesia seems to have disappeared with the detailed charting of anesthetic observations by anesthesiologists. Sudden unexpected death under anesthesia with negative postmortem findings is not an acceptable basis for the diagnosis of status lymphaticus.

Operating Room Study Commissions

To complement the Clinical Anesthesia Conference it is necessary to develop study commissions for the operating room in each state. The commission should organize study committees locally, mainly at county levels. It should be the primary objective of this commission to secure statistics on deaths, analyze the case reports, and classify them according to an agreed system.

The organization of this commission should be as follows. It should be under the aegis of the state medical society and, in turn, each functioning component, either district or county medical society, should have a working committee. These commissions together with their local committees are the responsibility of all physicians, not only of anesthesiologists. They should be composed of three primary specialists—an anesthesiologist, a surgeon, and a pathologist. The chairmanship should be rotated each year.

This commission should be an official committee of the medical society and the society should enlist the support and help of the medical examiner's office as well as the local bureau of vital statistics. Copies of death certificates representing deaths occurring in hospitals consequent to some medical procedure should be sent to the commission. Those which are pertinent should be analyzed and classified. Deaths considered to be pertinent are those occurring chiefly in the intraoperative period, defined as the entire period of preparation, preanesthetic medication, anesthesia, surgery, and postanesthetic and operative recovery up to 12 hours. Other deaths may be considered which are related to operation but are delayed.

The Need for Accurate Records of Deaths During Anesthesia.—The infrequency of autopsies seriously limits the definitive conclusions of anesthesia study committees. This situation could be readily corrected if every death occurring under anesthesia were followed by postmortem examination as regularly as are other deaths occurring due to accidental or unknown causes or under suspicious circumstances.

There is great need for accurate registration of deaths occurring during anesthesia and surgery by a central agency. (The phrase during anesthesia and surgery does not imply cause.) The data on such deaths have been buried in statistical tables, usually in the category of the primary condition for the relief of which the anesthesia and operation were intended. This practice is as valueless to the medical profession as the classification of deaths in automobile accidents would be to interested agencies if such deaths were listed under fracture of skull, for example, without mention of the automobile accident or the circumstances. Occasionally, but with more frequency, deaths associated with anesthesia have been classified as "accidental poisoning by opium derivatives or barbiturates," "inhalation of food or other object causing obstruction," "complications of anesthesia for nontherapeutic purpose," or "therapeutic misadventure in anesthesia" (International List of Causes of Death, no. E954). The last group is the only one which clearly denotes deaths occurring under anesthesia. In the report of the National Office of Vital Statistics for 1950, 76 deaths were classified as "therapeutic misadventure in anesthesia." Such are the unrealistic official statistics on deaths occurring under anesthesia. Since 43 "therapeutic misadventures in anesthesia" were listed in the National Summary of Deaths for the year 1949 (the first year in which they were segregated), one may infer that deaths under anesthesia are being reported more accurately or commonly. We hope that the correct explanation is the former one. In time, however, operating room study committees will be able to provide a more accurate picture of the true frequency of this occurrence.

The Problem of Cardiac Arrest

It appears to be the consensus that the term cardiac arrest has been widely misused in hospitals. This term constitutes a wastebasket for sudden and not-so-sudden deaths in the operating room. Many situations have been included which have well-defined etiological and pathogenic factors. In view of the confused situation and lack of definition it is desirable to discard this term and select one that does not have so many erroneous connotations and can be arbitrarily defined within specific limits. To this end, the term cardiocirculatory collapse has been suggested.

Partial List of Precipitating Factors of Cardiocirculatory Collapse

Indirect	Direct
Moribundity	Trauma to heart or pericardium
Anesthetic agents	Surgical contact
Hypoxia	Torsion of heart
CO_2 retention	Effusion
Blood loss	Pericarditis
Hypotension	Cardiac catheters
Reflexes—vagal	Electroconvulsive therapy
Diminished venous return	
Pooling of blood after mobilization of tumors	
Drugs, e. g., epinephrine	
Radiopaque dyes	
Electronarcosis	

Definition.—Cardiocirculatory collapse is a state of ineffective cardiac action resulting in inadequate cardiac output. It is iatrogenic, and it is apparently sudden and results in a state of clinical death.

The genesis of the state begins with recognition of a variety of inciting and sustaining factors, all of which drastically reduce cardiac output through one of three mechanisms: by weakening cardiac contractility, by producing ventricular fibrillation, or by causing cardiac standstill. Some of the precipitating causes are listed in the table. For purposes of nomenclature and statistical classification one can divide the entity into two parts, namely, the diagnostic and the causative components, and assign a code number to each. Thus, the diagnosis is "cardiocirculatory collapse" (code number), and the cause is "due to blank" (code number).

Limitations.—Inherent in the definition and genesis of cardiocirculatory collapse are a number of principles and selected aspects of the syndrome previously designated as cardiac arrest. First, it is recognized that cardiocirculatory collapse is not an etiological entity but a physiological end-state. It is the common end-result of the various factors listed and any others on which agreement can be reached. Above all, this condition is not a sudden divine act or "bolt out of the blue" but a culmination of various continuous, persistent derangements in physiology. Second, as a corollary to the first limitation, it is believed that many of the events preceding cardiocirculatory arrest are not always appreciated, recognized, or in some cases recorded. Although many of the factors are known, there may be subliminal stresses which must be identified. More careful observation and monitoring of patients may be necessary to indicate what is a contributing cause of collapse. Third, it is necessary to define cardiocirculatory collapse as an iatrogenic syndrome. This is clarified in terms of the inciting factors and circumstances. From a consideration of the etiological factors presented it is evident that they are oriented to or induced by the physician. They are either (1) related to actions or procedures performed by physicians on patients or (2) due to drugs administered by physicians to patients.

As a corollary to this fundamental point specific hospital areas where this iatrogenic syndrome is usually produced or occurs may be recognized. These are (*a*) the operating rooms; (*b*) the dental clinic; (*c*) the cardiorespiratory physiology laboratory, where cardiac catheterizations, bronchospirometry, and other diagnostic procedures of like nature are performed; (*d*) the radiology department, where mediums are injected to secure diagnostic information, with or without anesthesia, in such procedures as arteriography, aortography, and the making of pulmonary lipiodol studies; (*e*) the psychiatric unit, where electroconvulsive therapy is carried out, with or without anesthesia; and (*f*) miscellaneous units where local anesthetic drugs are administered for so-called minor procedures. These indeed cannot be called minor when fatalities are occasionally encountered.

Fourth, consideration must be given to the question of when cardiac resuscitation measures should be instituted. Cardiac resuscitation should be instituted in iatrogenically precipitated circumstances and not when the collapse is precipitated in purely medical situations or conditions by constitutional diseases. The rash of thoracotomies occurring in emergency rooms, medical wards, and even ambulances must be condemned generally. It has even been suggested by at least one expert that laymen should be taught the fundamentals of cardiac resuscitation and massage. In these attempts no thought is given to what is to be achieved or how it is to be achieved. The fundamental plan for successful resuscitation, namely, the restoration of the entire oxygen system, must be understood. In such a plan there are two requirements: 1. To provide artificial respiration by providing a proper airway and performing ventilation. This means that there must be adequate personnel with the proper skill and equipment, especially if a thoracotomy is to be done. 2. To provide artificial circulation by performing a proper thoracotomy and instituting cardiac compression. This means there should be present someone with surgical skill and knowledge of the technique of effective compression, including rate, force, and pattern. It is also necessary to be able to manage the open chest and to close it. These two components of the oxygen system are mutually dependent. One must certainly not attempt the second without the insurance and actual institution of the first; yet thoughtless thoracotomies are being performed without due consideration of the principles and in the face of inadequate assistance and equipment.

Furthermore, it has been emphasized that the chances of reviving a patient whose heart is compromised by intrinsic disease are rare. Indeed, in the operating room, where all skills are available and there is usually a preconceived plan of action, the incidence of successful resuscitation is nil in cases in which there is preexisting cardiac disease. If, under ideal circumstances, resuscitative efforts are not too successful, it is then inconceivable that thoracotomy and cardiac resuscitative efforts should be attempted on patients hospitalized for purely medical diseases when they suffer an acute cardiac episode. It is known that clinical survivals are rare but that biological survivals do occur and are termed vegetable. It is concluded that patients with medical conditions who suffer cardiocirculatory collapse should be allowed to die in peace instead of in pieces.

One additional aspect must be considered, namely, the moral. No physician is obligated to institute extraordinary measures to save life, especially under impossible circumstances. Indeed, it has been so indicated by at least one recognized authority on medical morals, namely, Pope Pius XII.[7] On Nov. 24, 1957, the pope was asked by delegates to the international congress of anesthetists in Rome the following question about artificial respiration: "Does the anesthetist have the right, or is he bound, in all cases of deep unconsciousness, even in those that are considered completely hopeless, to use modern artificial respiration equipment?"

He answered, "Since these forms of treatment go beyond the ordinary means to which one is bound, it cannot be held that there is an obligation to use them." In brief, in a case in which death is deemed certain and life can be prolonged only by artificial methods, the physician is not absolutely obliged to prolong life by extraordinary means. In answer to the question of when death occurs, the pope stated that, for theological purposes, "Human life continues for as long as its vital functions [clinical life] —distinguished from the simple life of the organs [biological life]—manifest themselves spontaneously . . . without the help of artificial processes [extraordinary]." However, the establishment of the exact instant of death is the task not of the church but of the physician.

In conclusion, this opinion seems reasonable. It was accepted by the anesthesiologists at the congress, and these physicians were of diverse faiths. Discussion with many other religious leaders further indicates a fairly widespread medical moral agreement.

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CLINICAL NOTES

USE OF ICE COLLAR IN PAROXYSMAL AURICULAR TACHYCARDIA

REPORT OF A CASE

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A 61-year-old man who had had frequent attacks of tachycardia since the age of 16 years was seen in the office with a regular apical rate of 172 per minute. His only complaints were "fast heart" and slight weakness.

He had been hospitalized in April, 1958, for tachycardia. At that time an electrocardiographic diagnosis of supraventricular tachycardia was made; the apical rhythm was regular and varied between 140 and 180 per minute. In the hospital the patient received an initial dose of 0.6 mg. of lanatoside C (Cedilanid) intravenously and another dose of 0.3 mg. two hours later. His rate then returned to normal, the total dose of lanatoside C during his hospitalization being 0.9 mg. On his discharge, digitalis in tablet form (Digiglusin) was prescribed. He then did well until the attack that brought him to the office, when it was assumed that the dosage of digitalis had become inadequate for maintenance.

In the office, pressure was applied to the carotid sinuses, 1½ grains (0.1 Gm.) of secobarbital (Seconal) was given by mouth, and the Valsalva maneuver was carried out, all to no avail. A rubber ice collar was then laid transversely, without any pressure, across the patient's neck at the level of the carotid sinuses as he lay supine. The ice collar had been kept in a refrigerator where a temperature of 38 F (3.3 C) was maintained. In approximately three seconds a normal rhythm of 60 beats per minute was established. The ice collar was then removed and a few minutes later, while the patient's blood pressure was being taken, it was noted that he again had tachycardia. The ice collar was reapplied as before, and the rate reverted to normal immediately. Thereafter, though the ice collar was removed, the normal rate persisted.

The rubber ice collar measured 3 by 4 by 12 in. (7.5 by 10 by 30.5 cm.) and weighed, with the water contained in it, 11 oz. (31 Gm.). The make used was no. 415 Davol Redi-Freeze. It was thought most likely that the result was a reflex from temperature receptors in the skin of the neck.

Box 365.

THROMBOCYTOPENIC PURPURA ASSOCIATED WITH HYDROCHLOROTHIAZIDE THERAPY

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Chlorothiazide and hydrochlorothiazide are widely used, effective, orally given nonmercurial diuretic and antihypertensive agents. A principal action of these drugs is marked enhancement of the excretion of sodium and chloride and to a lesser extent of potassium. Although they possess the advantage of being relatively safe drugs, there are a few side-reactions of importance, including nausea, skin rash, anorexia, headache, restlessness, and constipation. Potentially serious side-effects include postural hypotension; circulatory collapse; sodium, potassium, and chloride depletion; temporary aggravation of hyperuricemia; and acceleration of hepatic coma in patients with severe liver disease.[1] Two cases of purpura with thrombocytopenia due to administration of chlorothiazide (Diuril) have recently been reported.[2]

Among a group of patients treated with hydrochlorothiazide a case of thrombocytopenia with purpura presumed to be due to administration of this drug was encountered and is here described. The problem of purpura was complicated by adynamic ileus secondary to hypopotassemia.

Report of a Case

A 55-year-old woman was admitted to the hospital because of nausea, vomiting, and weakness. Six years previously she had been hospitalized for acute left-sided hemiplegia and was found to have rheumatic heart disease with mitral stenosis, auricular fibrillation, and congestive heart failure. She responded to treatment with mercurial diuretics and digitalis. Administration of quinidine was effective in converting the fibrillation to a normal sinus rhythm. At the end of three months some restoration of function of the paralyzed side had occurred. For the next four years her congestive heart failure was controlled with a low-sodium diet and treatment with mercurial diuretics and digitalis. Administration of quinidine was discontinued in 1954 because it was no longer effective, even in higher doses, in maintaining a normal sinus rhythm. Her only episodes of congestive heart failure usually corresponded to the occurrence of upper respiratory infections, to which she seemed peculiarly subject.

In May, 1958, she was started on treatment with chlorothiazide, 250 mg. twice daily. One month later she returned, generally improved and showing mild congestive failure. She complained of some reduction in appetite. She had taken no quinidine for four years; only digitoxin and chlorothiazide had been given as treatment. A few ecchymotic areas were noted on her legs and arms. A peripheral blood smear showed only slight reduction in platelets. The same schedule of medication, diet, and close observation was continued throughout the rest of 1958. Small ecchymotic areas were noted from time to time. Her general progress continued otherwise satisfactorily.

On Jan. 3, 1959, she was seen on an office visit and found to be in mild congestive failure. Treatment with chlorothiazide was discontinued and hydrochlorothiazide administration was started, 25 mg. twice daily. She was given an injection of 2 cc. of meralluride (Mercuhydrin) sodium intramuscularly and returned to her home. About eight hours after her visit to the office she complained of mild nausea and malaise, with anorexia and slight diarrhea. These symptoms continued with increased severity for about 10 hours and then abated temporarily for two weeks.

By Jan. 28 she was having unremitting nausea and vomiting and was admitted to the hospital, weighing 112 lb. (50.8 kg.). She was dehydrated and appeared to be in congestive heart failure. Her neck veins were full and her lips and nails were moderately cyanotic. An enlarged and moderately tender liver was palpated three fingerbreadths below the xiphoid process. The complete blood count indicated moderate hemoconcentration, with a hematocrit value of 45%; hemoglobin concentration 13.5 Gm.%; white blood cell count 12,000 per cubic millimeter; serum potassium level 2.74 mEq. per liter; and serum sodium level 124 mEq. per liter. Urinalysis was essentially normal.

X-ray studies of the abdomen showed adynamic ileus. Bloody diarrhea was noted. She was given potassium parenterally and the signs of hypopotassemia with muscle cramps, weakness, and ileus disappeared within eight hours. Oral alimentation was begun, along with efforts to maintain her electrolyte status.

On the fourth hospital day scattered ecchymotic and purpuric areas were observed on the lower extremities. A platelet count was noted to be 48,000 per cubic millimeter. Results of direct and indirect Coombs tests were negative. The patient showed symptomatic improvement, regained her strength, and took a normal low-sodium diet, with little if any gastrointestinal distress. Blood cultures taken

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on admission were reported as showing negative results. By the ninth hospital day the platelet count was 237,000 per cubic millimeter, hematocrit value 31%, hemoglobin concentration 9.4 Gm.%, and red blood cell count 3,050,000 per cubic millimeter. An L. E. test preparation was negative on the 12th hospital day. Her weight had increased to 125 lb. (55.4 kg.). She was discharged on Feb. 16 on therapy with digitoxin, 0.2 mg. daily; potassium supplement, 1 tsp. three times a day; a hematinic preparation of ferrous sulfate and molybdenum oxide, one tablet three times a day; a vitamin supplement twice a day; and hydrochlorothiazide, 25 mg. twice daily.

Five days after discharge she returned to the office, saying that she was "feeling fine" and with a platelet count of 319,000 per cubic millimeter and red blood cell count of 4,720,000 per cubic millimeter. She made good progress for two weeks and then developed a similar episode of nausea, vomiting, and diarrhea. When she reentered the hospital on March 13, 1959, her abdomen was distended and she was moderately dehydrated, weighing 118 lb. (53.5 kg.). The blood pressure was 140/80 mm. Hg, the apical rate was 72 per minute, and there were periods of bigeminy. One small area of mucosal purpura was noted in the buccal mucosa. There was an area of ecchymosis measuring about 6 by 10 cm. on the right thigh and several smaller areas of ecchymosis and purpura on both lower legs and both upper arms. The hematocrit value was 51%, with a hemoglobin concentration of 14.4 Gm.%, and 5,450,000 red blood cells per cubic millimeter. The white blood cell count was 23,400 per cubic millimeter, with 85% segmented neutrophils, 6% band neutrophils, and 9% lymphocytes. The platelet count was 38,159 per cubic millimeter and the serum potassium level was 3.3 mEq. per liter. The prothrombin time was 13 seconds, 85% of mean normal activity. Urinalysis was again normal.

Abdominal x-ray examination showed a normal gas pattern in the colon, with dilated loops of small intestine. The patient had one other episode of bloody diarrhea shortly after admission. Her response to parenterally given fluids and intravenous administration of potassium was rapid, and the next day the platelet count was 43,650 per cubic millimeter. The results of direct and indirect Coombs tests were again negative.

When she was discharged on March 23 the platelet count was 168,160 per cubic millimeter. She was sent home, taking the same schedule of medicaments as in February, except that hydrochlorothiazide was omitted. Four months later she was able to do light housework although still in mild chronic congestive heart failure which required administration of a mercurial diuretic at weekly intervals. There has been no recurrence of the purpura.

Investigative Studies

Studies were performed in an attempt to show the relationship, if any, between the thrombocytopenic purpura and the administration of hydrochlorothiazide.

Experiment 1: Platelet Levels After Administration of Hydrochlorothiazide.—It is evident that thrombocytopenia and purpura followed the institution and reinstitution of hydrochlorothiazide therapy. After administration of this drug was discontinued, the platelet count gradually returned to normal on both occasions while the patient was in the hospital. It appears that the hydrochlorothiazide was the only agent administered that could have been provocative, because when it was eliminated from the therapeutic program the patient remained free from purpura and thrombocytopenia. A third attempt to induce thrombocytopenia and purpura with hydrochlorothiazide was not carried out because of the fear of reinducing a more severe bleeding diathesis.

Experiment 2: Coombs' Test for Antibody-coated Platelets.—A suspension of the patient's platelets was prepared according to the method of Tullis.[3] Result of Coombs' test performed on a fresh platelet suspension was weakly positive. The addition of hydrochlorothiazide enhanced this reaction. Platelet lysis was also observed in this system. Performing this same procedure with chlorothiazide showed occasional small clumps of platelets like those seen in the mixture of Coombs' serum and the platelet-rich suspension. There appeared to be no enhancement of the agglutination by this drug.

Experiment 3: Effect of Hydrochlorothiazide on Clot Retraction.—It has been demonstrated that, if platelets are removed from plasma by centrifugation, clot retraction can be abolished. This same effect can be produced if the platelets are destroyed in vivo or in vitro by the action of potent antiplatelet serum.[4] In the case herein cited, if hydrochlorothiazide was the causative agent in producing this patient's thrombocytopenia and purpura, addition of hydrochlorothiazide to the blood of this patient convalescing from a drug-induced thrombocytopenic purpura should diminish clot retraction. A method was devised to estimate this reduction of clot retraction: 2.0 ml. of the patient's blood was added to 0.5 ml. of a saturated solution of hydrochlorothiazide in 0.9% saline solution in a small test tube. In another tube 2.0 ml. of the patient's blood was added to 0.5 ml. of 0.9% saline solution as a control. At the end of one hour complete retraction of the clot had developed in the control. There was no demonstrable clot retraction in the tube with hydrochlorothiazide.

Experiment 4: Demonstration of a Factor in the Patient's Serum, in Addition to the Hydrochlorothiazide, Necessary for the Agglutination of Plate-

lets.—Platelet-rich plasma from a person with a normal platelet count and testing serum from the patient with the hydrochlorothiazide-induced purpura were prepared according to the method of Harrington and co-workers.[5] To 0.1 ml. of platelet-rich plasma in each of a series of small test tubes the following preparations were added: in the first tube, 0.3 ml. of EDTA (disodium ethylenediamine tetraacetate acid)-treated heat-inactivated serum; in the second tube, 0.3 ml. of a saturated solution of hydrochlorothiazide; in the third tube, 0.3 ml. of a saturated solution of chlorothiazide; in the fourth tube, 0.3 ml. of the EDTA-treated heat-inactivated serum and 0.1 ml. of a saturated solution of hydrochlorothiazide; and in the fifth tube, 0.3 ml. of the EDTA-treated heat-inactivated serum and 0.1 ml. of a saturated solution of chlorothiazide. The tubes were agitated briefly and then allowed to incubate at 5 C (41 F) overnight. The next day the tubes were shaken gently to resuspend any sedimented platelets and part of the contents was poured onto a microscopic slide. The slides were kept in a moist atmosphere for 30 minutes and before examination agitated by hand for five minutes at about 40 rpm. Readings were made at high and low magnifications. The results are shown in the table.

Findings of Experiment to Demonstrate Agglutination Factor

Tube No.	Platelet-rich Plasma	Serum	Hydro-chloro-thiazide	Chloro-thiazide	Agglutination*
1...............	0.1	0.3	..	..	..
2...............	0.1	..	0.3	..	..
3...............	0.1	..	..	0.3	..
4...............	0.1	0.3	0.1	..	4
5...............	0.1	0.3	..	0.1	2

* *Agglutination was graded 1 to 4, with 4 the greatest. These results were confirmed by duplicate tests on two different occasions and observed by two examiners.*

Comment

Drug-induced thrombocytopenic purpura is becoming more prevalent, and the recognition of this entity is of considerable importance. As in some other drug-induced thrombocytopenic purpuras, the hemorrhagic manifestations were transitory in this case, and the patient required no specific treatment. Early recognition of a drug as a causal factor may render unnecessary the use of steroids or surgery, or both. Accepted practice demands that every adult patient with thrombocytopenic purpura be carefully questioned for the possibility of drug causation before the diagnosis of idiopathic thrombocytopenic purpura is made.

The effect of hydrochlorothiazide on this patient's platelets in the peripheral blood and in vitro has been demonstrated. The abnormality was shown to exist in the patient's serum in the presence of the offending drug. Normal platelets were agglutinated when the patient's serum was mixed with hydrochlorothiazide. In experiments 3 and 4 it was shown that the presence of both the patient's serum and the drug, hydrochlorothiazide, was necessary to bring about the abolition of clot retraction and platelet agglutination respectively. By the Coombs test both agglutination and lysis of platelets were demonstrated. In experiment 4 the presence of a factor in the patient's serum in addition to hydrochlorothiazide was demonstrated. The discrepancy between the weakly positive results of the Coombs test with chlorothiazide and the agglutination of normal platelets with the patient's serum in the presence of chlorothiazide as demonstrated in tube 5, experiment 4, is difficult to explain. Although in our initial experiments we were unable to demonstrate any enhancement of the reaction between Coombs' serum and the patient's platelets by the addition of chlorothiazide, it is possible that more quantitative procedures would have shown a greater degree of agglutination. The results of these experiments suggest a mechanism of sensitivity, i. e., an antigen-antibody type of reaction. By a series of more elaborate experiments with quinidine and allyl-isopropyl-acetylcarbamide (Sedormid), other workers[6] have considered that the drugs acting as haptenes unite with platelets and thereby confer antigenic properties on them. It seems justifiable to assume that this incident of thrombocytopenic purpura had a similar pathogenic mechanism.

While a rapid manifestation of purpura and thrombocytopenia after exposure to an offending drug is somewhat more common in drug-sensitive persons, clinical purpura and decreased platelet levels may be delayed for several days.[7] This delayed manifestation of purpura and gastrointestinal bleeding in the patient described is thus not without precedent. Since other drug precipitants have been carefully excluded, it appears justifiable to assume that the hydrochlorothiazide induced the thrombocytopenia and purpura in this patient. Severe thrombocytopenic purpura followed the institution of hydrochlorothiazide therapy in this patient. She recovered completely after discontinuation of the drug therapy. Reinstitution of hydrochlorothiazide therapy reproduced a similar episode of thrombocytopenia and purpura. This case therefore satisfies Ackroyd's[4a] criteria for the etiological demonstration of drug-induced thrombocytopenic purpura.

Summary

In the case of thrombocytopenic purpura reported here, the patient also had acute partial intestinal obstruction, with hypopotassemia as a secondary complication. Her response to electrolyte replacement and discontinuation of drug therapy was satisfactory. This case satisfies Ackroyd's[4a] criteria for drug-induced thrombocytopenic purpura. The possibility that the mechanism of hydrochlorothiazide-induced thrombocytopenic purpura is similar

to that of purpura induced by administration of quinidine or allyl-isopropyl-acetylcarbamide (Sedormid) is suggested.

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The chlorothiazide used in this study was supplied as Diuril by Merck Sharp & Dohme, Division of Merck & Co., Inc., Philadelphia; the hydrochlorothiazide was supplied as HydroDiuril by Merck Sharp & Dohme and as Esidrex by CIBA Pharmaceutical Products Inc., Summit, N. J.

Dr. Harold D. Palmer, pathologist, of Presbyterian Hospital, aided in the preparation of this report.

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COMMITTEE ON COSMETICS

Report to the Committee

The following paper was presented at the symposium, "The Management of Cutaneous Facial Disfigurements," in Atlantic City, June 9, 1959. This symposium was sponsored by the Committee on Cosmetics at the 108th Annual Meeting of the American Medical Association. This is the third in a series of papers, the first two of which appeared in THE JOURNAL, *Dec. 26, 1959, page 232, and Jan. 9, 1960, page 160.*

VERONICA LUCEY CONLEY, Ph.D., *Secretary.*

COSMETIC MANAGEMENT OF NEVI AND PIGMENTARY DISTURBANCES

Otto C. Stegmaier, M.D., Davenport, Iowa

Pigmented Nevi

Pigmented nevi, the common moles of the skin, are more appropriately called melanocytic nevi[1] since they are benign growths of melanocytes. They begin to appear in early childhood, when special collections of melanocytes at the epidermal-dermal junction become activated. New lesions may continue to develop up to puberty, and occasionally in adult life a shower of nevi may appear. Initially, the first lesions are pigmented macular dots, but after months or years they become elevated and acquire a variety of surface characteristics. In the fifth decade of life, some nevi, after undergoing fibrotic and fatty degeneration, may disappear.[2]

Histological examination of an early appearing nevus reveals the presence of growing melanocytes at the junction between the epidermis and dermis. This designated junctional activity occurs in 100% of all nevi in children,[3] 65% of all nevi in the third decade of life,[2] and dwindles to less than 10% in persons over 50 years of age.[4] Some nevi, however, do not mature and retain junctional proliferation throughout life. Junctional proliferation, instead of being considered a histological prerequisite for malignancy, should be considered a phase of the life cycle of the nevus. Nevertheless, if a melanoma arises from a nevus, and this has never been histologically proved, it usually develops at the junctional zone. Therefore, when a mole is removed, at least that portion of the tumor containing the epidermal-dermal junction should be preserved for future histopathological scrutiny. In most older nevi, the nevus cells are not connected to the epidermis but are confined to the dermis. These nevus cells are inactive and harmless.

Treatment.—All nevi showing changes in surface characteristics such as growth, color, and ulceration should be completely excised. For cosmetic reasons most nevi may easily be treated by shave excisions. The lesions are partially lifted above the skin by an injection of a local anesthetic. The elevated portion is shaved or sliced off level with the skin, and the bleeding base is coagulated. This method is relatively simple, the scar is minimal, and a histopathological record of the lesion is obtained. Walton, Sage, and Farber[5] have removed over 100 lesions by this method and, on reexamination of the sites

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of removal by excisional biopsy one to three years later, found no sign of malignant activity of the melanocytes or nevus cells. Apparently, nevi treated in this manner are completely removed initially, and, if not, the residual nevus cells are buried in the scar tissue. Pigmentation occasionally reappears after the removal. There is no need for alarm if this occurs, *since the pigment is due to migration of* benign melanocytes from the periphery of the scar.[6] The tissue removed should be examined by a pathologist extremely familiar with pigmented skin tumors. Otherwise, a false positive report may result in mutilating surgery.

Vitiligo

Vitiligo is a defect caused by tyrosinase, resulting in the failure of melanin production.[7] It is apparently inherited. The condition affects certain melanocytes, causing localized areas of depigmentation, occasionally segmental and, rarely, generalized. It is easily recognizable in persons with dark skins. Because of the lack of contrast in light-skinned persons, vitiligo can be recognized more easily by the use of the filtered long-wave (3600 A) Wood's light. Vitiligo may be confused with post-inflammatory leukodermas and with leukodermas due to external application of chemicals, with no demonstrable preceding inflammation. It may also be confused with the following depigmentary abnormalities: depigmentation after contact with monobenzone (Benoquin) and guanofuracin (about the eyes), partial depigmentation secondary to patchy eczema in children, tinea versicolor, and localized albinism. The latter condition, the most difficult to differentiate from vitiligo, begins at birth and is frequently associated with a white forelock.

The main problem of the patient with vitiligo is the cosmetic disfigurement. The psychological effects are, of course, greatest in the Negro, Indian, Asiatic, and dark Caucasian. In India, where the condition is sometimes confused with leprosy, vitiligo carries a severe social stigma. Recently, the Indian government announced that research funds would be allotted to the treatment of three conditions, leprosy, malaria, and vitiligo. "Because of the disfigurement, the physician cannot dismiss this disease as a mere cosmetic problem without realizing the important psychological complications that occur."[7]

Treatment.—The primary object in the treatment of vitiligo is to restore pigment to the white areas or to minimize the contrast between the normal skin and the vitiliginous or depigmented skin. Obviously, in a fair skinned person, who has minimal vitiligo and who is not exposed to much sunlight, there is no need for treatment.

In contrast to this patient, the dark person with extensive vitiligo on the exposed skin needs help. For patients with vitiligo in whom over 75 or 80% of the exposed areas are depigmented, it has been recommended that monobenzone ointment be used for bleaching the rest of the skin.[8] However, the depigmenting effect of this material is rather varied. It works in some persons but not in others. Quite often, its depigmenting effect is uneven and, therefore, cosmetically disadvantageous. Furthermore, local application of monobenzone frequently causes eczematous sensitization. This may take many months (applications twice daily). Allergic reactions *may occur. After this exposed skin is depigmented,* occasional applications of this ointment are necessary to maintain it in the depigmented condition. To prevent severe burning after exposure to sunlight, the local application of a sun-screen cream or lotion is needed. The use of the psoralens as oral, sun-protective medicaments may also be indicated.

Since most patients with vitiligo do not fit into the two previously mentioned groups, some other form of therapy is needed. It has been shown that ingestion of the photosensitizer, methoxsalen (Meloxine, Oxsoralen), together with repeated exposures of the affected parts to sunlight, will induce pigment formation in some areas of vitiligo. Whether the photosensitization reaction affects the tyrosinase molecule per se or whether the result is due to the epidermal and dermal inflammation is not known. Becker[9] believes that the metabolic block is broken by the inflammation. The treatment is tedious, unpredictable, and prolonged. Sunlight is more effective than artificial ultraviolet rays, although, recently, I[10] have induced partial pigmentation of areas of vitiligo after the patient's ingestion of methoxsalen and his exposure to fluorescent bulbs emitting exclusively long-wave ultraviolet light (over 3200 A). It is also apparent that in the southern latitudes the treatment is more effective, probably as a result of more hours and greater intensity of sunlight as pointed out by Elliott.[11] Nevertheless, probably less than 10% of the patients can expect a result that could be considered cosmetically acceptable. It has also been shown by Elliott[11] that, unless treatment is maintained after the repigmentation, the pigmentation will eventually regress; so, for the present time, this method of treatment must be prolonged indefinitely. Becker[9] believes that vitiligo is the result of a metabolic tyrosinase block. According to him, the skin reactions of patients after the use of methoxsalen and sunlight will vary with the completeness of the enzyme block as follows: "In some patients absolutely nothing happens. Some patients pigment slightly in summer and lose all the pigment the next winter. Treatment here is a waste of time. Some patients pigment in the summer and retain the pigment through the next winter. Here pigment can be added each year. Occasionally, a vitiligo patient can be cured in a month—obviously the enzyme block was labile."

Method.—A dosage of 20 mg. of methoxsalen is taken orally two hours before exposure to sunlight. The patient's exposure time should be limited to 15 minutes on the first day and then increased 5 minutes a day on successive days or at least three times a week. This should be continued for at least two months during the summer. If pigment returns and does not fade in the winter, further therapy the next summer is worthwhile. As the artificial sources of near-ultraviolet light are perfected, continuous therapy during the winter months may be feasible.

Toxicity.—Extensive trials of methoxsalen over a 10-year period have not revealed definite toxicity.[12] However, its effects on persons with chronic illnesses of the liver, kidney, or gastrointestinal tract have not been thoroughly investigated. This medicament should not be used in a patient with any of these chronic diseases. Since methoxsalen is a powerful photosensitizer, it is not known if prolonged usage will increase the incidence of skin cancers. Clinical experience to date does not indicate it. (The stratum corneum of the epidermis thickens, and more pigment accumulates in the skin after the patient's exposure to ultraviolet light when this is preceded by the oral administration of methoxsalen. It is thought that this increased ultraviolet-blocking effect produced by methoxsalen should decrease rather than increase the carcinogenic effect of this drug.)

Chloasma

Chloasma is a localized hyperpigmentation of the face. It may occur during pregnancy or after encephalitis, or there may be no detectable cause. Chloasma must be differentiated from isolated hyperpigmented spots of different origin, e. g., from spots arising after local application of photosensitizing compounds contained in perfumes and cosmetics. Initially, chloasma occurs because there is increased production of melanin. Later, the lesion may persist because melanin is being retained by the melanocytes.

Treatment.—Since we do not know the precise mechanism causing chloasma, treatment is unsatisfactory. Systemic therapy is of no value, although large doses of vitamin C have been recommended. A pigment inhibitor, monobenzone, has been used for local application.[13] It is of some value when there is active pigment formation, but it will not clear up all cases of chloasma. Since it stops pigment formation, it must be used intermittently or a white spot may result. Ito,[14] Becker,[9] and Spencer[15] have indicated that persistent white areas may remain if the patient becomes allergic to the locally applied medicament. This has occurred in Oriental persons and Negroes. Spencer[15] has succeeded experimentally in producing persistent white spots, both in the areas treated and in other areas distant from the treatment site. For these reasons, the application of a 10% concentration of monobenzone is not recommended for colored persons and is to be used with extreme caution in others.

Peeling preparations such as 5% salicylic acid in alcohol or 5% ammoniated mercury may lighten the pigment. Additional darkening of the areas due to the sun may be prevented by the application of sun-screen vanishing creams or lotions. The benzophenones (10% in vanishing cream) will filter out all ultraviolet rays up to 4000 A.[16] The tetra-substituted benzophenones are apparently a better absorbing compound than are the di-substituted benzophenones for the near-ultraviolet rays. The latter rays cause darkening of preformed leukomelanin in the skin. The rays that stimulate erythema and pigment formation are also filtered out. Since the benzophenones filter out all of the middle and near-ultraviolet rays, they should prevent the darkening of chloasma which is most noticeable in the summer. Creams and solid stick forms of foundation makeup can be used to hide the blemishes. These preparations are waterproof and are available in various shades to match the skin color.

Summary

Moles can be safely and easily removed by shave excision and coagulation of the base of the lesion. Examination of the tissue should be made by pathologists familiar with pigmented skin tumors. Vitiligo and chloasma may be treated in a variety of ways, none of which is completely successful in all persons.

Benzophenones (Uvinuls) may be obtained from Antara Chemicals Division, General Aniline and Film Corporation, 435 Hudson Street, New York. Cyasorb is a similar compound obtained from American Cyanamid Co., Rockefeller Center, New York.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN CEREBRAL VASCULAR ACCIDENTS

George A. Wolf Jr., M.D., Burlington, Vt.

Cerebral vascular accidents may be defined as sudden events occurring in the cerebrum caused by diseases of the blood vessels. Simple description of the various types of accidents and discussion of differential diagnosis are beyond the scope of this paper.

Structural and Functional Considerations

Several anatomic and physiological facts are important to consider in discussing treatment of the more common types of cerebral vascular accidents. Effective collateral circulation is possible in the brain. Vasospasm, with resultant structural defects, has been observed. Sludging of blood as a transient phenomenon has been observed in superficial arteries. The humoral and nervous control of circulation in the brain is highly developed. Disease of the blood vessels in the brain is manifest clinically by the secondary effects on functioning nervous tissue. Moreover, at autopsy, the secondary effects overshadow or obscure the primary blood vessel lesion.

These features complicate the evaluation of the effects of therapy, especially if the therapy is directed at the relief of transient episodes. For example, in thrombotic disease, is a good result of treatment caused by (1) abolition of spasm, (2) establishment of collateral circulation, (3) prevention of extension of a thrombus, (4) relief of sludging, (5) other factors, or (6) a combination of factors?

Our basic knowledge of the pathophysiology of cerebral disease is lacking. Thus, attempts to alter the disease processes are purely empirical, and the interpretation of results is inaccurate.

Clinical Considerations

Possibly, the most common cerebral vascular accidents are (1) transient cerebral ischemia, (2) cerebral arterial thrombosis, (3) cerebral arterial embolism, (4) cerebral hemorrhage associated with hypertension, and (5) cerebral artery aneurysm of the berry type associated with rupture. The differential diagnosis of these conditions is admittedly difficult. Cerebral hemorrhage associated with hypertension is usually fatal. Cerebral artery aneurysm requires arteriography and possibly surgery.

During the past few years, attention has been focused on the occurrence of arteriosclerotic plaques and thrombi, either in the common carotid artery or the proximal part of the internal carotid artery, as the cause of impaired circulation to the brain. In those instances in which symptoms of hemiparesis come on slowly, consideration should be given to this diagnosis. Here again, arteriography followed by surgery, in appropriate instances, is indicated. The medical treatment of transient cerebral ischemia and cerebral arterial thrombosis and embolism is to be considered here. Once damage to the cerebral nervous tissue is established, as evidenced by persistent neurological defects, nothing yet known can change the lesion in the brain. Treatment is supportive during the acute phase of a cerebral vascular accident and rehabilitative when the defects stabilize. Attention to coexisting disease, the complications of immobility, and the stress of acute illness are important in all patients. Techniques are available for strengthening weakened muscles and returning many seriously handicapped patients to productive or at least self-sufficient living.

Drugs To Consider in Treatment of Cerebral Vascular Accidents

Anticoagulants.—Patients with cerebral vascular accidents of any type, who may develop peripheral venous thrombosis or mural thrombi and (if myocardial infarction is a complication) who may subsequently develop emboli to the lungs and other sites of infarction, can be protected by the use of anticoagulants and the mortality from the disease reduced. However, the use of anticoagulants in cerebral vascular disease must be evaluated in terms, not of the death rate, but of the effect on the cerebral lesion, if possible. Since, in bleeding aneurysms or cerebral hemorrhage, the use of anticoagulant therapy would hasten the patient's death, it is evident that anticoagulants can be used only in selected cases.

Dean and Professor of Clinical Medicine, College of Medicine, University of Vermont.

The use of bishydroxycoumarin (Dicumarol) and related long-term anticoagulants has received a great deal of attention lately. Theoretically, it has much to recommend it in some instances. If a diseased area of the vascular system is such as to favor fragile clot formation, so that particles of coagulated blood (emboli) break off into the systemic circulation and travel to the cerebral vasculature, adequate anticoagulant therapy maintained until the vascular disease is cured or arrested should theoretically prevent the formation of further emboli and prevent further cerebral vascular occlusion and brain infarction. There would appear to be excellent theoretical reasons and strongly suggestive clinical observations supporting the notion that, in proved cases of cerebral embolization, anticoagulants should be given under close supervision for a prolonged period. For example, bishydroxycoumarin given in sufficient doses to maintain the prothrombin level in a therapeutic range should be maintained for a period of not less than six months. Blood prothrombin determinations should be done every 7 to 10 days. To specify a prothrombin level in terms of per cent of normal is hazardous. Figures varying from 10 to 40% of normal are recommended by different authorities. The physician should consult with the laboratory which is to perform the test. It is preferable that the determinations be performed always in the same laboratory and by the same method. The physician should determine from this consultation what the appropriate prothrombin level to produce reduced coagulability should be, according to the standards of the laboratory.

Heparin sodium (Heparin Sodium, Liquaemin Sodium) may be used in urgent situations in which embolic episodes are occurring at frequent intervals. Although it is difficult to prove in an individual patient that the embolic phenomena did not terminate spontaneously, it would appear that the foregoing type of therapy is the preferred method of treatment at the present time.

If a clot or thrombus has formed in a small branch of a cerebral artery or a vein, as the result of disease of that artery or vein, and if insufficient time has elapsed to allow endothelization of the intravascular surface of the clot, the thrombus may act as a nidus for the growth and extension of the thrombus. Obstruction of a larger vessel may result, with more extensive or clinically apparent brain damage. Theoretically, a decrease in the coagulability of the blood would reduce the likelihood of growth or extension of the thrombus. It has been postulated in some instances that sludging can occur temporarily and result in cerebral ischemia without thrombosis. Although the mechanism of sludging has been observed in certain superficial vessels, no data are available on its occurrence in the cerebral circulation.

With the aforementioned two theoretical principles in mind, physicians are apparently prepared to treat two common forms of cerebral vascular accident, i. e., thrombosis and transient cerebral ischemia. Although experience is increasing, controlled studies proving the effectiveness of these two theoretical uses of anticoagulants have not yet been accomplished. Clinical experience, however, suggests that anticoagulants are worth a trial in well-defined cerebral arteritis of an infectious or chemical etiology with thrombosis, in order to prevent extension of the thrombus formation.

The use of anticoagulant drugs in the patient with cerebral arterial thrombosis associated with atherosclerosis theoretically might be of value in preventing the extension of the thrombus, as was indicated. However, difficulties in differential diagnosis of this disorder and intracranial hemorrhage make its use hazardous.

Furthermore, in any proposed use of an anticoagulant in the prophylactic care of cerebral vascular accidents, individual consideration must be given to weighing the good likely to be accomplished against the possibility of dangerous bleeding from unsuspected sources. Whether from dietary inadequacies or constitutional differences, patients vary greatly in their response to anticoagulants, and assurance must be had that prothrombin determinations will be consistently reliable and frequent enough to determine and maintain safe dosage.

There would seem to be agreement that, when a fully developed stroke or complete neurological syndrome occurs as the result of intravascular cerebral thrombosis, the use of anticoagulants for the purpose of preventing further strokes is not justified.

The problem revolves around the treatment of transient, minor strokes which have the potentiality of recurring or extending. Not only is it difficult to be sure of the etiology of the so-called minor stroke, but its differentiation from other forms of neurological disease by the average physician is difficult.

It is also difficult to contemplate treating all older patients, who have transient episodes of giddiness and transient numbness and tingling and other minor neurological symptoms, with anticoagulants for periods up to six months. Yet, in a given case, if these symptoms are truly prodromata of an impending cerebral vascular accident of the thrombotic type, anticoagulants theoretically would be indicated.

In my opinion, the use of anticoagulants in the treatment of cerebral vascular accidents should be confined to the type of cases in which well-controlled studies have shown the drug to be effective, i. e., cerebral embolism and chemical or infectious arteritis. Certainly, a few successful trials of this method of treatment by the individual physician is poor indication that the drug is useful.

Fibrinolysins.—The use of fibrinolysins to dissolve thrombi has not been tried successfully in the therapy of cerebral vascular thromboses.

Vasodilators.—One of the unknowns in the pathophysiology of cerebral vascular disease is the role of vasospasm, either in the production of impaired neural function without infarction or in neural damage produced by a thrombus or embolus and its resultant ischemia. That gross spasm in cerebral blood vessels can occur has been demonstrated, but a serious question can be raised as to whether this is good or bad for the patient. In subarachnoid hemorrhage, blood vessel spasm may offer some protective hemostasis to the patient. In the pale infarct stage resulting from thrombosis, vasospasm may contribute to the size and growth of the infarct. Furthermore, it must not be assumed that absence of spasm improves circulation in the brain. Indeed, there is experimental evidence to suggest that vasodilatation may reduce blood flow to certain areas.

Stellate ganglion block has been used extensively but, for the most part, is losing favor. The absence of controlled studies, the difficulty of evaluating its effect on a transient phenomenon, the theory behind its use, and the complications, e. g., pneumothorax, indicate it should not be used freely or by inexperienced hands.

Numerous chemical vasodilators are available, but, considering the precise control of the cerebral circulation by neural and humoral mechanisms, vasodilators with an effect on the systemic circulation would probably act peripherally before a cerebral effect is manifest, and the net result might be reduced blood flow.

Possibly the safest vasodilator known to have an effect on the cerebral vessels is carbon dioxide. This drug, used by inhalation over a period of a few minutes, can be tried in an attempt to produce a beneficial effect. If it is ineffective, it can be withdrawn immediately.

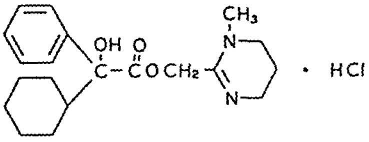
Miscellaneous Drugs.—To date, drugs that are useful in prevention or definitive treatment of cerebral vascular accidents are not available. Miscellaneous drugs are involved occasionally in the treatment of patients with cerebral vascular accidents, but the use of these has to be adjusted to the individual case. The routine use of antibiotics to prevent pneumonia should be restricted to those patients in whom the likelihood of pneumonia is high. Morphine should be avoided completely because of the effect of this drug on the respiratory center. Indeed, drugs which tend to alter the state of consciousness should be avoided insofar as possible. For the control of extreme restlessness, paraldehyde remains the drug of choice. Attention should be paid to general supportive measures such as diet, electrolyte and fluid balance, and bladder, skin, and bowel care.

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Oxyphencyclimine Hydrochloride (Daricon).—(1-Methyl-1,4,5,6-tetrahydro-2-pyrimidyl)methyl α-cyclohexyl-α-phenylglycolate hydrochloride. — The structural formula of oxyphencyclimine hydrochloride may be represented as follows:



Actions and Uses.—Oxyphencyclimine hydrochloride, an anticholinergic agent, is used clinically as an adjunct in the management of peptic ulcer.

Oxyphencyclimine hydrochloride is basically atropine-like in action. Thus, in animals, it produces mydriasis, inhibits salivation, lacrimation, and pancreatic secretion, and decreases the tone and amplitude of intestinal contractions. It diminishes both total and free gastric hydrochloric acid secretion, whether spontaneous or provoked by histamine or a test meal, and inhibits the development of experimental ulcers. The action of oxyphencyclimine is largely peripheral; usual doses neither block transmission in ganglions nor exert a curare-like action on the myoneural junction of skeletal muscle. It does, however, antagonize tremors produced by 1,1′-(2-butynylene)dipyrrolidine(tremorine), presumably by an action within the central nervous system.

As an adjunct to diet, rest, and antacids, oxyphencyclimine hydrochloride may afford symptomatic relief from the pain of peptic ulcer, with an accompanying suppression of gastric motility and a decrease in the volume and acidity of gastric secretion. When compared to other atropine-like drugs, it appears to have a relatively long duration of action; after oral administration, effects appear within 1 to 2 hours, become maximal in 6 to 8 hours, and persist for as long as 12 hours.

Side-effects reported are, for the most part, similar to those of other anticholinergic drugs: dryness of the mouth, blurred vision, constipation, urinary hesitancy or retention, and, less frequently, drowsiness, palpitation, and increased ocular tension. These symptoms are often satisfactorily controlled by reducing the dose.

Like other atropine-like drugs, oxyphencyclimine hydrochloride is contraindicated in patients with glaucoma and should be used with caution in the presence of prostatic hypertrophy, cardiospasm, or pyloric obstruction.

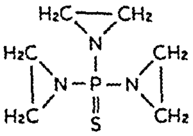
Dosage.—Oxyphencyclimine hydrochloride is administered orally. The usual dose is 10 mg. given twice daily. If the response is inadequate, the total daily dosage may be gradually increased up to 50 mg. (given in divided amounts) unless prohibitive side-effects supervene. The dosage should be adjusted for each patient to achieve maximal benefit without undue toxicity.

Preparations.—tablets 10 mg.

Year of introduction: 1958.

Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of oxyphencyclimine hydrochloride.

Thio-Tepa (Thio-Tepa).—*tris*(1-Aziridinyl)phosphine sulfide.—N,N′,N″-Triethylenethiophosphoramide.—The structural formula of thio-tepa may be represented as follows:



Actions and Uses.—Thio-tepa, a polyfunctioning alkylating agent, is used for the palliative management of certain malignant diseases. There are no qualitative differences in its action on normal and tumor cells from those observed with nitrogen mustard (HN_2), triethylene melamine (TEM), and chlorambucil. Since, however, it is not a vesicant and can be placed in solution at a pH which is not irritating to the tissues, thio-tepa can be given by all parenteral routes. The drug has a slower onset of action than the other alkylating agents, but immediate side-effects, such as nausea and vomiting, are minimal.

Thio-tepa has been tried in the palliation of a large variety of neoplastic diseases. Results have been variable, and there is a wide divergence of opinion as to the relative effectiveness and proper area of usefulness of this drug in comparison with other alkylating agents. Apparently, the choice of chemotherapeutic agents and the sequence in which they are used depend, in large measure, on prior experience and personal preference. In general, however, thio-tepa may be considered a nitrogen mustard-like drug with clinical applications similar to this class of drugs. There seems to be fairly consistent, but not unanimous, agreement by experts that thio-tepa is not the initial treatment of choice in any malignant neoplasm. Rather, it probably should be withheld until further surgical and radiation (x-ray or isotope) therapy is no longer effective or feasible; it is ordinarily not used for early or localized lesions. Owing to the lag between administration of thio-tepa and tumor response, the drug is of limited value for the acute complications or phases of far advanced neoplastic diseases. In favorable cases, the duration of remission is variable, and, in common with other anti-neoplastic agents, subsequent courses of therapy with thio-tepa are usually less effective than the previous ones.

Clinical experience with thio-tepa has been greater in epithelial (carcinomatous) tumors than in any other type of malignant disease. Present evidence indicates that the drug has a definite place in the therapy of metastatic carcinoma of the ovary and breast. Because it can be given by intraserosal injection, thio-tepa is helpful in the control of persistent serous effusions associated with such lesions. Results seem to be better in patients with pleural and pericardial effusion than in those with peritoneal effusion (ascites). It is difficult to know whether chemotherapy in such cases actually prolongs life. However, satisfactory remissions, with objective and symptomatic improvement, have been observed in many instances. Thus, the judicious use of thio-tepa may make existence more comfortable in patients with widespread ovarian and mammary carcinoma when radiation and hormonal therapy no longer afford palliation.

The drug has been tried in a number of patients with disseminated bronchogenic carcinoma, and, in occasional instances, it has provided brief periods of remission. Given either by carotid artery injection or intracerebrally (directly into the brain at the time of surgery or through a bur hole), thio-tepa has been used with some beneficial effect in a small number of patients with cerebral metastases. There are sporadic reports of transient remissions after the use of thio-tepa in patients with other carcinomas. In many cases, the drug has been injected directly into the tumor mass as, for example, into breast lesions and by perianal infiltration into obstructive lesions of the anus and rectum. Thio-tepa has shown little promise for the palliation of carcinomas of the gastrointestinal tract, head and neck, prostate, kidney, liver, biliary tract, or pancreas.

Both chronic granulocytic and lymphocytic leukemia may respond to thio-tepa, the results being better in the former than in the latter. Most workers in the field seem to feel that radiation therapy is preferable for the initial treatment of chronic leukemia. The role of thio-tepa in radiation-resistant cases is less well defined. Thus, in chronic granulocytic leukemia, some hematologists advocate busulfan as the first choice of available chemotherapeutic agents; others prefer thio-tepa. Likewise, in patients with chronic lymphocytic leukemia, the drug can be used in the same manner as mechlorethamine, triethylene melamine, or chlorambucil, but there is no general agreement as to which agent is preferable or should be used first. Thio-tepa is of no value and should not be used in acute leukemias. Results of therapy in malignant lymphoma (principally lymphosarcoma and Hodgkin's disease), while limited, indicate that thio-tepa is probably of the same order of effectiveness as nitrogen mustard and related alkylating agents. The drug has been tried in melanosarcoma (malignant melanoma), but, despite a few favorable reports, it has been generally disappointing for this purpose.

Recently, some investigators have proposed the administration of thio-tepa and other alkylating agents at the time of cancer surgery and in the immediate postoperative period, in an attempt to augment surgical palliation and to diminish seeding due to surgery. In the laboratory, such use of the drug has been observed to decrease the number of "takes" of implanted tumors in experimental animals. Clinical experience, however, is far too limited to permit the routine recommendation of alkylating agents for this purpose, either at the time of palliative or curative surgery. Only further study will establish whether such agents are beneficial from the standpoint of over-all cancer mortality and incidence of postsurgical neoplastic recurrence. Hence, this procedure, which carries with it an appreciable added risk to the patient, must be considered experimental.

Toxicity and Side-Effects.—Thio-tepa is a drug of high toxicity for the hematopoietic system. The drug affects all of the formed elements of the peripheral blood. Thus, lymphopenia followed by neutropenia and thrombocytopenia may attend its use; erythrocyte depression is variable. The effects on bone marrow are unpredictable; rarely, maximum depression occurs as late as 30 days after therapy has been discontinued. In some cases, irreversible hypoplastic anemia has occurred. The necessity for continuous maintenance therapy involves the hazard of potentially serious adverse effects on bone marrow. It is imperative that the hematological status of the patient be carefully observed during, and for some time after, therapy. The hemoglobin level and leukocyte and platelet counts should be determined daily during the first week or 10 days of treatment, once a week while the patient is receiving maintenance therapy, and for four weeks after discontinuance of medication. Any significant changes in these elements of the blood necessitate prompt assessment of the erythrocyte level and a differential leukocyte count. When the leukocyte and/or platelet counts have fallen to 4,000 or 150,000 respectively, either therapy should be discontinued or the dosage greatly reduced. Thio-tepa should be given cautiously, if at all, to patients whose bone marrow has been depressed by direct invasion of tumor cells or by previous therapy with ionizing radiation or other cytotoxic drugs. It is contraindicated in pregnant women because of serious adverse effects on the fetus.

Nausea, vomiting, anorexia, and headache are the principal side-effects of thio-tepa. Since gastrointestinal symptoms are less frequent and less severe than with other nitrogen mustard-like drugs, one should never attempt to gauge therapy by the dose required to produce emesis, as has been suggested for other agents of this type. Febrile and allergic reactions are occasionally encountered with administration of thio-tepa. Intestinal perforation through cytolysis within a lesion might occur. The drug has also been observed to produce amenorrhea in the female and diminished spermatogenesis in the male.

Caution is again enjoined in the use of thio-tepa. Because of its cumulative and unpredictable toxic effects on bone marrow, the drug is best reserved for use by physicians experienced in the chemotherapeutic management of malignant disease.

Dosage.—Thio-tepa can be administered by the following routes: intravenous, intra-arterial, intramuscular, intratumor (direct, transrectal, transvaginal, intracerebral) and intraserosal (pleural, pericardial, peritoneal), or by combinations of these. Dosage can never be given empirically—it must be completely individualized or titrated for each patient according to the hematological and clinical response. It should be emphasized that thio-tepa has a slow onset of action and a cumulative toxic effect on the bone marrow. Thus, a delayed response to the drug may be deceptive and occasion an unwarranted frequency of administration, with subsequent signs of toxicity. Maintenance therapy should be no more frequent than once every one to three weeks in order to allow for better evaluation of the hematological picture.

Although there is no "usual" dose for intravenous, intra-arterial, or intramuscular injection, most authorities agree that the maximum daily dose for the initiation of therapy by these routes is 0.2 mg. per kilogram of body weight. Such dosage should be continued no longer than five days, even though no changes in the peripheral blood have become apparent. Depending on subsequent clinical and hematological response, therapy may then be cautiously resumed. The maximum maintenance dose is 0.2 mg. per kilogram of body weight per week. For intracarotid use in patients with cerebral lesions, doses as high as 40 to 50 mg. have been given and repeated at intervals of six to nine weeks.

For local tumor injection, amounts ranging from 10 to 60 mg. have been given in single or multiple sites.

For intraserosal use in patients with serous effusions secondary to metastatic lesions, doses of 10 to 50 mg. have been injected into the pleural, pericardial, and peritoneal cavities after paracentesis. The dose can be repeated when fluid reaccumulates.

For the treatment of leukemia, dosage is governed not only by the clinical and hematological response but also by the severity of the disease prior to initiation of therapy. In general, the higher the leukocyte count the greater the amount of drug required. This is only a general rule, however, and each case must be considered individually, keeping in mind the unpredictable response of diseased bone marrow to drugs of this type. Particular caution is enjoined in patients with chronic lymphocytic leukemia since this type of the disease is generally more sensitive to cytotoxic agents than is chronic granulocytic leukemia. For the initiation of therapy, doses ranging from 10 to 60 mg. or more are given (usually by intravenous injection) over a period of five days. Maintenance therapy is carried out on a weekly to triweekly schedule in doses no larger than 10 mg.

Powdered, sterile preparations of thio-tepa should be stored in the refrigerator and, after reconstitution with sterile water for injection, used immediately. Unused solutions should be discarded.

Preparations.—powder (injection) 15 mg.

Year of introduction: 1959.

Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of thio-tepa.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The Council has authorized publication of the following report.

Philip L. White, Sc.D., *Secretary.*

OVERUSE OF MILK IN THE DIETS OF INFANTS AND CHILDREN

Clement A. Smith, M.D., Boston

Milk is traditionally stated to be the best food for infants, or "the most nearly perfect food." Although such statements may be true, it does not follow that other foods are unnecessary or that no limit needs to be placed on the milk intake. At frequent intervals it is necessary to call attention to the occasional overuse of milk in the feeding of infants and to suggest means by which such overuse may be avoided. The misuse of milk may be well illustrated by the record of a patient at the Children's Hospital, Boston. Individual features of this story could be matched from the records of any children's clinic in the United States today. Their association in one patient is especially interesting and educational.

Report of a Case

A boy, 21 months of age, was brought to the outpatient department of Children's Hospital in August, 1958. His mother complained that the child had attacks of ". . . . losing his breath and stiffening, since 4 to 5 months of age, and appeared anemic." The attacks in which he lost his breath had occurred ". . . every time the baby was frightened, angry, or reprimanded," from an original frequency of every two to three days to a current rate of three to four times daily. He had never fallen or hurt himself during these attacks because his mother was always there to catch and hold him until he breathed or cried, ". . . a few seconds later." The father, a service man on emergency call, had irregular hours of sleeping; therefore, the child ". . . since birth, was never permitted to cry for fear of waking the father."

Delivery had been at term, after a normal pregnancy of a healthy mother. Birth weight was 5 lb. 10 oz. (2,551 Gm.). There had been no illnesses, with the exception of an upper respiratory infection at four months of age. There had been no known blood loss. The patient was formula fed and had no difficulties with feeding except ". . . refusal to eat solid foods," which led to a daily intake of approximately 48 oz. (1,500 cc.) of milk. The mother urged this upon the child by bottles between meals and by cup at meal times. Meat and orange juice had been accepted sparingly for the preceding few months. No supplemental vitamins had been given since the age of 14 months. Development included sitting alone at 7 months, walking at 14 months, and a few words of speech at 18 months of age.

Physical examination included weight and height measurements, which were at the 25th percentile for normal boys of his age. He weighed 24 lb. 12 oz. (11.2 kg.). The child's pallor, rounded face, and curly blonde hair gave the first impression that he was a girl. Additional significant findings were a normal heart size, with regular sinus rhythm, pulmonic second sound louder than aortic, and a grade 2 systolic murmur along the left sternal border. Liver edge was palpable but no other abdominal viscera were felt. Neuromuscular findings were

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From the Department of Pediatrics, Harvard Medical School.

A transfusion of 120 ml. of packed cells was given on the first day because of the severity of the anemia. Fruit juice, fortified with 250 mg. of both iron (ferrous sulfate) and ascorbic acid, was given between meals three times daily. Milk, except when used on cereals, was omitted from the child's diet so that his appetite for other foods would be increased. Solid food, juices, and water were offered for not over 30 minutes three times daily. A sample day's diet included: juice, toast, egg, banana, and corn flakes for breakfast; fruit, chicken or other meat, dark green or yellow vegetable, and potato for lunch; cereal, toast, fruit, and orange juice for supper. The child gradually began to eat better despite a weight loss of 12 oz. (340 Gm.). By the end of the week he was eating solids fairly well and only occasionally did he skip a meal.

At no time was any breath-holding or loss of consciousness observed during his hospital stay. When discharged after six days, the child's hemoglobin concentration was 7.6 Gm. per 100 ml. His condition was diagnosed as hypochromic microcytic anemia due to a deficiency of iron and conduct disturbance manifested by breath-holding (according to history). On a follow-up visit to the outpatient clinic six days later, the child was eating well at his own pace, had gained approximately 1 lb. (454 Gm.), and had not resumed his breath-holding spells. The systolic murmur and some pallor were still present, but other examination findings were negative. Hemoglobin concentration was found to be 8.6 Gm. per 100 ml. The mother was told to continue the iron and ascorbic acid medication until a subsequent check-up and to reintroduce milk at meal times, but only in amounts not interfering with the consumption of a varied diet of solid foods.

This case history reveals more than one result of ill-advised behavior by a compulsive mother. Clearly, she believed her child should not cry, should not go hungry, and should get plenty of milk. All these are proper maternal objectives with limitations, but like most good objectives all of them can be carried to harmful extremes. There is extensive literature available on the contribution of milk to the diets of infants and children.[1] For example, the Children's Bureau Publication, "Your Child from One to Six" states that [2]: "As the child grows older, milk still contributes more than any other single food although it is relatively less important than it was during the first year of life. Milk is outstanding as a source of the mineral calcium and the vitamin riboflavin and is also a good source of the best quality of protein, of vitamin A, and of thiamine (vitamin B_1)."

Role of Milk in Children's Diets

Milk as a food for the growing child should be considered only as to interrelationships of the child's protein, calcium, and iron needs and the amounts of these nutrients in milk. Current interest in the possible effects of various fats upon the arteries is too recent for any information to have appeared on the relationship between such foods in infancy and the vascular system in adult life. The data in table 2 show that the child of 1 to 3 years of age who receives all or most of his caloric requirement from milk will get only a small fraction of the iron his growing body needs. Surprisingly, iron deficiency anemia is seen almost as often today as it was 20 years ago.[3] The fact that it is seen at all in these times of mass health education is surprising, but may be partly a result of improper

TABLE 2.—*Nutritional Value of Cow's Milk**

Nutrient	Amount in 1 Qt. of Cow's Milk	Recommended Daily Allowance for Child of†			
		2-6 Mo.	7-12 Mo.	1-3 Yr.	10-12 Yr.
Protein, Gm.	35	...	...	40	70
Calcium, Gm.	1	0.6	0.8	1	1.2
Iron, mg.	0.4-0.5	5	7	7	12
Vitamin A, I.U.	1,600	1,500	1,500	2,000	4,500
Vitamin D, I.U.	400	400	400	400	400
Riboflavin, mg.	1.6	0.5	0.8	1	1.8
Thiamine, mg.	0.4	0.4	0.5	0.7	1.3
Niacin, mg.	1.0	6‡	7‡	8‡	17‡
Ascorbic acid, mg	14	30	30	35	75
Calories	640	kg ×120	kg.×100	1,300	2,500

* Homogenized Vitamin D milk.

† The Food and Nutrition Board recognizes that human milk is the natural food for infants and feels that breast feeding is the best and desired procedure for meeting nutrient requirements in the first months of life. No allowances are stated for the first month of life. Breast feeding is particularly indicated during the first month when infants show handicaps in homeostasis due to different rates of maturation of digestive, excretory, and endocrine functions. Recommendations as listed pertain to nutrient intake as afforded by cow's milk formulas and supplementary foods given the infant when breast feeding is terminated. Allowances are not given for protein during infancy. (Recommended Dietary Allowances, Publication 589, National Academy of Sciences, National Research Council, Food and Nutrition Board, rev., 1958.)

‡ Milligram equivalents.

health education. Overemphasis on any single food or on any individual nutrient (such as calcium and phosphorus) to the extent that others may be neglected, should be avoided.

The amount of protein in cow's milk would appear to be adequate, as seen in table 2, and to judge by paired feeding experiments[1a] its quality is as useful for supporting growth in young animals as an equal amount of protein from other sources. Lynch,[4] citing McCance,[5] has raised some questions as to the proper level of protein intake at which calcium is best absorbed in adults. As shown in table 2, milk furnishes almost exactly that ratio of calcium to protein recommended by the Food and Nutrition Board for the diet of the child under 3 years of age. Later in childhood, sufficient milk to meet the calcium recommendation would not meet the need for protein (and for other nutrients as well, including calories). However, milk is much less likely to replace other foods in later childhood than during infancy. Thus, the limitation of cow's milk is the insufficiency of its iron content for hematopoiesis during infancy and early childhood.

This limitation is probably overlooked (thus contributing to the high incidence of iron deficiency today) because of three factors: (1) the widespread belief that milk is a perfect food, of which every child needs a quart a day; (2) overemphasis on demand feeding and the use of a bottle as long as the child wishes it; and (3) the belief that children should not be allowed to cry.

The attitude and the role of the physician in advising as to good nutrition for infants and small children may be modeled on another quotation from the Children's Bureau publication:[2]

> The preschool child is somewhat less dependent on milk for these essential nutrients than when he was a baby because he is eating a wider variety of foods. Some preschool children will continue to take a quart a day and keep a good appetite for other foods; they should have the full quart but no more. If a preschool child takes three cups of milk readily and has a good appetite for the other important foods in his diet, he is probably getting enough milk. A few children will not take more than one pint voluntarily and if they are persuaded to drink three to four cups of milk will not eat enough other foods. Under these circumstances, the doctor should be consulted to see whether the child is getting all the nourishment he needs from the combination of milk and other foods.

The physician and members of allied professions should not wait to be consulted by mothers regarding the feeding of their children. Some advice about the child's food should be volunteered at any check-up visit to the physician's office or at any well-child conference. It is interesting to consider how the opening remarks about milk or any other "good" food are usually phrased. Too often, the question asked is: "Does he get plenty of milk?" or, "I hope he drinks a lot of milk." Either question implies a recommendation of unlimited amounts. The better approach is: "How much milk does he get?" or "How much milk does he want?" If the mother then counters with "How much should he have?" a recommendation of any exact intake is as difficult to make and as likely to be wrong as any other form of dogmatism in regard to the normal. The basic premise is that the *nutrition of children* should be governed by general principles rather than by arbitrary rules. The management which results in a healthy and positive attitude toward a flexible and varied diet is preferable to compulsiveness toward a narrow regimen.

The answer to the mother's question: "How much milk should my child have a day?" should not be the statement of any quantity, but rather an inquiry into the child's diet as a whole. The milk intake should be considered in its relationship to intake of iron-supplying foods; such as egg yolk, lean meat, vegetables, and fruits. Normally, the milk intake recommended can be "somewhere between two and four cups altogether," since many mothers think of the milk intake only as that drunk and forget that consumed in other foods. Most physicians or child health clinics will have printed literature to be given to mothers, or they will have posters illustrating these general principles on display in waiting rooms. It is recommended that any such visual educational material be phrased carefully to avoid such words as "must have," "at least," and "every day." This avoidance of specific regulations is a basic element in all child guidance and habit formation. It may be that a physician who inculcates in a mother a noncompulsive attitude toward milk or any other dietary item also may be building a better mother-child relationship in general.

Summary

Milk is occasionally fed to infants or children in such excessive amounts that other essential foods, notably those providing iron, may be excluded. Such errors, which may result from medical emphasis on unlimited consumption of any good food, should be avoided by adherence to good general principles of nutrition.

References

1. (*a*) Anderson, Z. E.; Teply, L. J.; and Derse, P. H.: Nutritive Value of Representative Good American Diet With and Without Milk, Quart. Rev. Pediat. **12**:151-163 (Aug.) 1957. (*b*) Stearns, G.: Human Requirement of Calcium, Phosphorus, and Magnesium, chap. 4, Handbook of Nutrition, Symposium Prepared Under the Auspices of the Council on Foods and Nutrition of the American Medical Association, New York, the Blakiston Company, 1951. (*c*) Wilson, J. R.: Quart of Milk a Day, Cow's Milk as Source of Childhood Nutrients, Quart. Rev. Pediat. **8**:219-223 (Nov.) 1953.

2. Faegre, M. J.; Chandler, C. A.; and Hesseltine, M. M.: Your Child from One to Six, Publication 30, Children's Bureau, United States Department of Labor, 1945.

3. Diamond, L. K.: Personal communication to the author.

4. Lynch, H. D.: Use and Abuse of Milk, M. Sc. **1**:10 (Jan.) 1957.

5. McCance, R. A.; Widdowson, E. M.; and Lehmann, H.: Effect of Protein Intake on Absorption of Calcium and Magnesium, Biochem. J. **36**:686-691 (Sept.) 1942.

negative. The hemoglobin concentration was measured at once because of the child's pallor and was found to be 4.3 Gm. per 100 ml. The infant was promptly admitted to the ward for study and treatment. The laboratory findings are given in table 1.

The child remained in the hospital for a week. A transfusion of 120 ml. of packed cells was given on the first day because of the severity of the anemia. Fruit juice, fortified with 250 mg. of both iron (ferrous sulfate) and ascorbic acid, was given between meals three times daily. Milk, except when used on cereals, was omitted from the child's diet so that his appetite for other foods would be increased. Solid food, juices, and water were offered for not over 30 minutes three times daily. A sample day's diet included: juice, toast, egg, banana, and corn flakes for breakfast; fruit, chicken or other meat, dark green or yellow vegetable, and potato for lunch; cereal, toast, fruit, and orange juice for supper. The child gradually began to eat better despite a weight loss of 12 oz. (340 Gm.). By the end of the week he was eating solids fairly well and only occasionally did he skip a meal.

TABLE 1.—*Laboratory Findings on Patient in Children's Hospital*

Hematocrit reading	16%
Red blood cell count	3,400,000/cu. mm.
Mean corpuscular volume	47 cubic microns
Mean corpuscular hemoglobin (MCH)	12.6 micromicrograms
Mean corpuscular hemoglobin concentration (MCHC)	27 Gm./100 ml.
Total protein level	7.3 Gm.
Albumin	5.8 Gm.
Globulin	1.5 Gm.
Urine examination	Negative
Tuberculin test	Negative (1/1,000)
Chest film	Normal (except for borderline enlargement of heart shadow)
Electrocardiogram	Normal
Electroencephalogram	Normal

At no time was any breath-holding or loss of consciousness observed during his hospital stay. When discharged after six days, the child's hemoglobin concentration was 7.6 Gm. per 100 ml. His condition was diagnosed as hypochromic microcytic anemia due to a deficiency of iron and conduct disturbance manifested by breath-holding (according to history). On a follow-up visit to the outpatient clinic six days later, the child was eating well at his own pace, had gained approximately 1 lb. (454 Gm.), and had not resumed his breath-holding spells. The systolic murmur and some pallor were still present, but other examination findings were negative. Hemoglobin concentration was found to be 8.6 Gm. per 100 ml. The mother was told to continue the iron and ascorbic acid medication until a subsequent check-up and to reintroduce milk at meal times, but only in amounts not interfering with the consumption of a varied diet of solid foods.

This case history reveals more than one result of ill-advised behavior by a compulsive mother. Clearly, she believed her child should not cry, should not go hungry, and should get plenty of milk. All these are proper maternal objectives with limitations, but like most good objectives all of them can be carried to harmful extremes. There is extensive literature available on the contribution of milk to the diets of infants and children.[1] For example, the Children's Bureau Publication, "Your Child from One to Six" states that [2]: "As the child grows older, milk still contributes more than any other single food although it is relatively less important than it was during the first year of life. Milk is outstanding as a source of the mineral calcium and the vitamin riboflavin and is also a good source of the best quality of protein, of vitamin A, and of thiamine (vitamin B_1)."

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References

1. (*a*) Anderson, Z. E.; Teply, L. J.; and Derse, P. H.: Nutritive Value of Representative Good American Diet With and Without Milk, Quart. Rev. Pediat. **12:**151-163 (Aug.) 1957. (*b*) Stearns, G.: Human Requirement of Calcium, Phosphorus, and Magnesium, chap. 4, Handbook of Nutrition, Symposium Prepared Under the Auspices of the Council on Foods and Nutrition of the American Medical Association, New York, the Blakiston Company, 1951. (*c*) Wilson, J. R.: Quart of Milk a Day, Cow's Milk as Source of Childhood Nutrients, Quart. Rev. Pediat. **8:**219-223 (Nov.) 1953.

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THE JOURNAL
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UNSAFE AT HOME

FOR centuries the word home and its connotations have been synonymous with safety and security. This is expressed in the commonly used phrase "safe at home." Current accident records, especially involving children but by no means excluding adults, indicate the necessity for revised thinking. Home has become decidedly an unsafe place.

Recent events in the news emphasize the dangers which lurk in the home. Within the past 12 months there have been waves of publicity relating to deaths due to suffocation in plastic bags among infants and children, to fatalities and morbidity from lead poisoning due to the ingestion of fumes from wooden battery cases used for fuel, and to inadequate ventilation for widely used space heaters, leading to carbon monoxide poisoning, particularly in house trailers. The recognition of unused refrigerators as asphyxiating hazards to children dates back only a few years and is a continuing potential hazard.

These more or less spectacular eruptions of interest merely serve to focus attention on the growing hazards attached to living in the modern home. Many of these have appeared without fanfare, incidental to the introduction of labor-saving machinery and the application of modern chemistry to home cleaning and sanitation problems.

The substitution of detergents for soap has enhanced the efficiency of many cleansing operations, but it has also increased irritative and allergic reactions and introduced a new hazard of poisoning, to say nothing of depriving parents of a handy substance for washing out the mouths of small boys who indulge in bad language. Useful but caustic chemicals have helped to keep drains and soil pipes cleaner but continue to be a source of possible poisoning or caustic injury to delicate tissues such as conjunctivas and mucuous membranes. Garden chemicals for weed and pest control pose an ever increasing problem in accidental poisoning, especially when these are carelessly stored in milk or soft drink bottles.

The hazard of carbon monoxide poisoning is not limited to trailers and shack homes. Even the modern heating system, if improperly vented, may feed back carbon monoxide into the home, as may gasoline motors left running unattended in closed, attached garages.

The dangers involved in increased use of potent drugs, particularly self-medication with barbiturates and other sleeping tablets, are increasing rather than diminishing despite warnings by medical and public health authorities.

The recent ban on cranberries potentially contaminated by a chemical used for weed control focuses new attention on the possible hazards resulting from weed and pest control sprays and from food additives. The fact that some of these may be carcinogens adds a new emphasis to the poisoning hazard and carries with it an unfortunate overtone of panic.

The multiplicity of labor-saving devices now fills the home with heavier electric currents and more rapidly moving machinery. Do-it-yourself equipment, particularly power tools, creates additional dangers, especially in the hands of the unskillful. The homemade extension and the frayed electric cord continue to threaten electrocution of the unwary.

Despite slowly declining home accident rates, a new look at safety in the home is certainly indicated. This should be in a spirit of inquiry, evaluation, and prevention rather than panic. Unreasoning fear of all foodstuffs, all chemicals, and all labor-saving devices is no solution to the problem. Progress will not be turned back, and progress has always exacted its toll in human lives. There is a demand on health and safety officials, the medical profession, educators, and enlightened public leaders to render progress toward easier living as safe as possible. The responsibility is particularly heavy on the manufacturers and distributors of potentially dangerous substances and devices, on the public officials charged with the responsibility for their control, and on the medical profession for devising and publicizing means of prevention as well as for developing effective treatment.

There is evidence that responsible leaders in all of these groups are aware of the problem and are taking constructive steps to meet it. Probably the most important and the most difficult step is the alerting of an indifferent public without creating needless panic and unwarranted fears.

SUMMARIES IN INTERLINGUA

Of the few languages which are sufficiently diffused to play an international role in medical writing, English is far in the lead. Not only is it the native tongue of over 250 million people but it occupies a major place in foreign language study throughout Europe, and in Russia, India, Japan, South America, and elsewhere. It is often the vehicle for original communications in Scandinavian, Indian, Japanese, and South American medical journals. Thus it seems well on the way to becoming a world language. However, a recent survey, made under the auspices of UNESCO, indicates that it still falls far short of this goal, since only about one-half of the world's scientists are at present able to read English. For the other half a readable translation of a summary is needed so that they can appraise the contents of an English article and determine whether it merits a laborious and sometimes costly translation.

Numerous medical journals have met this problem by furnishing translations of summaries in several languages. No one objects to this procedure, nor can anybody deny its usefulness, but the problem of procuring good translations and of allocating space is often a bar to adopting this multilanguage approach. An alternate solution would be to use only one language for translation. But which language should be used? The one with the widest possible range of immediate comprehensibility should be favored. The UNESCO study provided the rather startling information that, of all existing languages, Interlingua has the widest range of immediate intelligibility. It is estimated that, in the case of medical literature, Interlingua textbooks have about twice the range of English textbooks and that they can be understood in almost all parts of the world where the Latin alphabet is used. Thus, an English summary with an Interlingua translation provides the widest as well as the most compact form of communication feasible in the present linguistic situation. For these reasons, the editors of THE JOURNAL have decided to follow the policy of 14 American and 6 foreign journals which regularly supply Interlingua translations of their summaries. These will appear each week in the advertising pages.

This action does not imply ignorance of the limitations which Interlingua shares with other languages, such as English, as a medium for international communication. Interlingua summaries will serve no useful purpose for most of our subscribers in the United States or for individual subscribers abroad who would not subscribe to THE JOURNAL unless they could read it. In the medical libraries of the world, however, the Interlingua summaries will be permanently available for the benefit of those who have an imperfect reading knowledge of English. Their facility in reading it will vary according to their language backgrounds. Those with a Romance language as their mother tongue will grasp it at first sight. Others in Europe, on both sides of the iron curtain, will do almost as well. So far, few or no factual data are available as to its scope in Russia, but the international technical-scientific vocabulary, which is the backbone of Interlingua, is known to be widely diffused in the Russian language. Any facility in reading Interlingua in the near and far East will depend mainly on a previous study of European language and would therefore not be great.

However, Interlingua could serve as a bridge from nonoccidental scientific literature. If a medical writer in Moscow, Istanbul, Cairo, Peking, or Tokyo were to present his material in Interlingua or prepare an Interlingua summary, he would speak to the rest of the world with a single voice so that his contribution would be immediately intelligible to the occidental world. This is not our problem.

The editors welcome comments on the usefulness of the new summaries. Interlingua is on trial as a practical adjunct primarily for foreign readers. Critical comments are anticipated from conservative and gifted linguists to whom Interlingua will appear as an easy way out of the translation problem. That is exactly what it is.

THE PHYSICIAN FROM THE ISLE OF COS

Plato has recorded a dialogue between Socrates and Hippocrates, in "Protagoras," which confirms the general belief that the father of medicine was a member of the inner circle during the golden age of Greece. Hippocrates was born on the island of Cos (Kos), one of the Dodecanese, about 460 B.C. His contemporaries included, among the notables, the philosopher, Aristotle; the sculptors, Polycletus and Phidias; the historians, Herodotus and Thucydides; the poet, Pindar; and the playwrights, Aeschylus, Sophocles, Euripides, and Aristophanes. Hippocrates was the 19th descendant of Asclepius and a member of the Asclepiadae, a guild of physicians, priests of the temples of Asclepius. The volume of medical literature of and concerning Hippocrates probably exceeds that of any physician, with the possible exception of Sir William Osler. More than 20 years ago, Ralph A. Major, professor of medicine at the University of Kansas School of Medicine, prepared a scholarly

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1. Major, R. H.: Hippocrates and Isle of Cos, Bull. Soc. M. Hist. 5:323-394 (June) 1946.
2. Katz, A. M.: Hippocrates and Plane Tree on Island of Kos, A. M. A. Arch. Int. Med. 104:653-657 (Oct.) 1959.

travelogue of his visit to the isle of Cos.[1] Major sailed on an Italian vessel from Brindisi, which carried him through the Corinthian Canal, with a stop at Piraeus, the port of Athens. Undoubtedly the preference for an Italian vessel was related to the annexation, in 1912, by Italy, of several Greek islands within the bosom of the mainland of Asia Minor. The international transfer followed the victory of Italy over Turkey at the conclusion of the Italo-Turkish War of 1911-1912. The Dodecanese remained under Italian sovereignty until 1947 when they were returned to Greece.

The modern traveler to the island will probably choose the standard five-day round trip from Piraeus, which includes Crete, Rhodes, Cos, Patmos, Delos, and Myconos. This trip is especially recommended for the physician who seeks rest and quiet through a Mediterranean cruise this winter. The boat to the islands is one of ancient vintage, in keeping with the points of interest. Six hours are spent on the island of Cos. The peaks of interest are the Asclepian temple on the outskirts of the village and the plane tree of Hippocrates near the agora.[2] The terraces of the temple have been reconstructed with a considerable quantity of the original stone. They provide an impressive skeleton image of the famous shrine built nearly 2,500 years ago. A spring flowing from one of the lower terraces may well have been the sacred spring used by Hippocrates in the healing rituals.

The plane tree in the center of the village is famous as the site for the Hippocratic lectures. The Hippocratic oath is inscribed (in Italian) on a tablet at the base of the tree. If this plane tree is the same one that sheltered Hippocrates, its age compares favorably with that of the giant redwoods of California. It is possible that the tree also served as an umbrella for St. Luke and St. Paul, the itinerant apostles. The tree today is supported by columns of marble and granite taken from the temple of Asclepius. In contrast, a Moslem mosque, with a single minaret, is visible nearby. It was built during the long reign of the Ottoman Turks. Extensive Roman ruins are passed on the return to the boat. These, being relatively modern, are spurned by present-day Greek antiquarians; they are less than 2,000 years old.

To Hippocrates has been credited the clinical system of rational experience and common sense, which anticipated the new era of medicine in the ancient world. The earliest shrine of Asclepius that has been identified was built in about 350 B.C. The great temple of Asclepius on the island of Cos was started only a few years later. By the second century B.C. coins from Cos bore a portrait of Asclepius leaning on the serpent's staff. In the early days of the Roman empire, but after the birth of Christ, coins were minted in Rome and in Cos which showed a seated figure with the inscription "Hippocrates."

Hippocrates was a seasoned traveler throughout the Near East. Undoubtedly he visited and practiced in parts of modern Athens, which included the Acropolis and Hadrian's gate in the center of the city. Athenian citizenship was conferred on him, one of the great honors of that time. On the southern slope of the Acropolis the remains of a temple of Asclepius are visible. This was erected in celebration of the end of the plague in 430 B.C. Stone images of the lungs, a leg, and an arm have been preserved; these are votive offerings, replicas of the area or organ cured. It is possible that they were used at times for the teaching of anatomy.

There are three other areas in Greece of interest to the medical rover. Three hours, by motor, south of Athens at Sounian on the tip of a rocky promontory is the temple of Poseidon, one of the gods credited by some with being the father of Asclepius. The prevailing opinion, however, favors Apollo as his father. From the promontory one may look across the sea toward the Cyclades islands. West of Athens lie the famous ruins of Delphi at the base of Mount Parnassus. Delphi is a traveler's must for the physician as well as the archeologist. Immediately below the temple of Apollo at Delphi, a few minutes by foot, is the Marmaria, a circular marble temple of Athena Pronolas. Also, one may inspect the altars to Athena Hygeia and to the goddess of birth, Eileithyia.

Southeast from Athens, across the Corinthian canal and into the Peloponnesus, the route leads to the birthplace of Asclepius, adjacent to the temple and amphitheater at Epidaurus. The amphitheater is in a remarkably fine state of preservation. Yet another Asclepian temple may be seen on the Acropolis in Corinth on the return to Athens. Also at Corinth is the temple of Aphrodite, goddess of sexual proficiency before the discovery of male and female hormones. The only obvious disappontment on the Peloponnesus was the absence of any ruins on the plains of Olympia, the site of the ancient Olympic games. Nor were there any remains of Sparta, home of the virile competitors of the Athenians.

Hippocrates is believed to have died in Thessaly. There is some evidence to suggest that he was a centenarian. The influence of Hippocrates as a disciple in the cult of Asclepius remained strong until the second century A.D. By this time Christianity had gained the balance of prestige. The last inscription preserved from Epidaurus was dated 355 A.D., commemorating the destruction of the temple of Asclepius. A short time later the last vestiges of paganism as a potent influence were stamped out.

RURAL HEALTH CONFERENCE

NATIONAL CONFERENCE ON RURAL HEALTH

The Council on Rural Health of the American Medical Association, in coöperation with state medical societies, national farm groups, agricultural leaders, and allied organizations, will hold its Fifteenth National Conference on Rural Health at the Pantlind Hotel, Grand Rapids, Mich., Feb. 25-27, 1960. The general theme chosen for this meeting is "Meeting Challenges With Responsibility." The program follows:

THURSDAY MORNING, FEB. 25

Carll S. Mundy, M.D., *Presiding*

8:00 **Registration**
No registration fee

9:45 **Opening Service**
Community Singing
DeVere A. Fader, Director of Music, Haslett High School, Haslett, Mich.
Donna Sue George, Junior, Haslett High School, Haslett, Mich.

10:00 **Invocation**
Rev. James W. Wright, Pastor, First Methodist Church, Grand Rapids, Mich.

10:05 **Greetings**
The Honorable G. Mennen Williams, Governor of the State of Michigan, Lansing.
The Honorable Stanley J. Davis, Mayor of the City of Grand Rapids, Mich.
Milton A. Darling, M. D., President, Michigan State Medical Society, Detroit.
Marvin L. Niehuss, President, Michigan Health Council, Vice-president and Dean of Faculties, University of Michigan, Ann Arbor.
E. K. Yantes, M.D., Council on Rural Health, American Medical Association, Wilmington, Ohio.

10:45 **The Two-Way Road**
F. A. Humphrey, M.D., Chairman, Council on Rural Health, American Medical Association, Fort Collins, Colo.

11:10 ***Meeting Challenges with Responsibility***
Glenn Cunningham, Ph.D., Cedar Creek Ranch, Cedar Point, Kan.

11:50 **Discussion Leader**
Oliver Ebel, Executive Secretary, Kansas State Medical Society, Topeka, Kan.

11:55 **Luncheon Period**

THURSDAY AFTERNOON

Allen T. Stewart, M.D., *Presiding*

1:30 **Community Singing**

1:35 **Panel: Careers in the Field of Medicine**
Moderator: Frank Mayfield, M.D., President, Ohio State Medical Association, Cincinnati.

1:50 **Student Nurse:**
Sally Ward, St. Mary's Hospital, Dale, Ind., Recipient of Nursing Scholarship, Woman's Auxiliary to the Indiana State Medical Association.

2:00 **Discussion**

2:15 **Dental Student:**
Robert L. Card, Senior, University of Michigan, Ann Arbor.

2:25 **Discussion**

2:35 **Medical Technology Student:**
Susan Sweet, Senior, Medical Technology, Michigan State University, East Lansing.

2:50 **Discussion**

3:05 **Medical Student:**
David J. Brecount, *Senior, University of Cincinnati*, College of Medicine.

3:15 **Discussion**

3:30 **Health Educator:**
Wallace Ann Wesley, Hs.D., Department of Health Education, American Medical Association, Chicago.

3:50 **Discussion**

4:05 **Impressions After Five Years of Rural Practice**
Jack L. Gibbs, M.D., Havana, Ill., Recipient of scholarship between Illinois Agricultural Association and Illinois State Medical Society.

4:45 **Discussion**

THURSDAY EVENING

F. S. Crockett, M.D., *Presiding*

8:00 **Musical Interlude**
Jerry Skinner, Senior, Eastern High School, Lansing, Mich.

8:15 **International Understanding**
Mrs. W. Wyan Washburn and W. Wyan Washburn, M.D., Council on Rural Health, American Medical Association, Boiling Springs, N. C.

FRIDAY MORNING, FEB. 26

Charles R. Henry, M.D., *Presiding*

9:00 **Community Singing**

9:05 **Panel: The Best Years of Our Lives**
Moderator: Frederick C. Swartz, M.D., Chairman, Committee on Aging, Council on Medical Service, American Medical Association, Lansing, Mich.
Panel Members:

9:15 Adolph M. Hutter, M.D., Fond du Lac, Wis.

9:25 Marvin A. Anderson, Ph.D., Associate Director, Agricultural Extension Service, Iowa State College, Ames.

9:35 Arthur Kemp, Ph.D., Director, Department of Economic Research, American Medical Association, Chicago.

9:45 William J. Brake, Chairman, Interim Health Committee, the National Grange, Lansing, Mich.

9:55 Samuel P. Leinbach, M.D., Council on Rural Health, American Medical Association, Belmond, Iowa.

10:05 T. J. Hitch, President, Tennessee Farm Bureau Federation, Columbia.

10:15 **Discussion**

11:30 **Summary—Must Time Take Its Toll?**
Theodore G. Klumpp, M.D., President, Winthrop Laboratories, New York.

12:00 **Luncheon Period**

FRIDAY AFTERNOON

W. WYAN WASHBURN, M.D., *Presiding*
"What Are We Eating?"
2:05 Do We Really Know?
DENA C. CEDARQUIST, Ph.D., Head, Department of Foods and Nutrition, Michigan State University, East Lansing.
2:35 Food For Thought For Life
ROBERT J. SAMP, M.D., the University of Wisconsin University Hospitals, Madison.
3:05 Discussion
3:30 Livestock and Livestock Products
S. L. KALISON, D.V.M., Extension Veterinarian, Virginia Polytechnic Institute, Blacksburg, Va.
4:00 Discussion
4:20 Quacks—In Foods and Drugs
OLIVER FIELD, Director, Department of Investigation, American Medical Association, Chicago.
4:50 Discussion

FRIDAY EVENING

F. A. HUMPHREY, M.D., *Presiding*

7:00 Banquet Invocation
Rt. Reverend Msgr. CHARLES W. POPELL, Chancellor, Grand Rapids Diocese, Pastor, St. Andrews Cathedral, Grand Rapids, Mich.
INTRODUCTION OF SPECIAL GUESTS
Greetings
Mrs. FRANK GASTINEAU, President, Woman's Auxiliary, American Medical Association, Indianapolis, Ind.
EMIL POLLARD, National Treasurer, Student American Medical Association, University of Michigan, Ann Arbor.
The Heart of the Challenge
E. VINCENT ASKEY, M.D., President-elect, American Medical Association, Los Angeles.

SATURDAY MORNING, FEB. 27

NORMAN H. GARDNER, M.D., *Presiding*

9:00 Community Singing
9:05 What Is Good Growth?
PAUL M. BANCROFT, M.D., Lincoln, Neb.
9:45 Discussion
10:10 Life-Span Immunization
JOHN D. PORTERFIELD, M.D., Deputy Surgeon General, Department of Health, Education, and Welfare, Public Health Service, Washington, D. C.
10:55 Discussion
11:15 This Is My Task
MRS. HAVEN SMITH, Chairman, Women's Committee, American Farm Bureau Federation, Chappell, Neb.
11:50 Adjournment

ORGANIZATION SECTION

2,683 VIEW FILM PROGRAM AT DALLAS MEETING

Ralph Creer, Director of Medical Motion Pictures and Television, reports that a total of 2,683 physicians viewed the films shown on the regular motion picture program during the A. M. A. Clinical Meeting in Dallas.

On the basis of attendance, the eight most popular films and their authors were as follows: "Complete Office Gynecological Examination," by Frederick Hofmeister, Milwaukee; "Routine Pelvic Examination," by S. B. Gusberg, New York; "Cardiac Arrest," by John Beard, London; "Total Hysterectomy," by Somers Sturgis, Boston; "Diagnosis and Treatment of Depressions," by Bernard Wortis, New York; "Physical Examination of the Newborn," by Mary Olney, San Francisco; "Just Four Minutes (Resuscitation for Cardiac Arrest)," by Lenore R. Zohman, Valhalla, N. Y.; and "Early Detection and Medical Management of Ulcerative Colitis," by Nicholas C. Hightower Jr., A. Compton Broders Jr., Henry Laurens, and Richard D. Haines, Temple, Texas.

ECONOMIC RESEARCH ADVISORY COMMITTEE

An Economic Research Advisory Committee in the Socioeconomic Division, composed of outstanding professional personnel, has been appointed. The Economic Research Advisory Committee serves in this capacity to the American Medical Association's Department of Economic Research under the direction of Arthur Kemp. The committee is charged with the basic responsibility of encouraging and fostering economic research programs and studies that are significant to the professional practice of medicine. The programs will be undertaken outside the American Medical Association by independent scholars or independent organizations engaged in professional research. The Advisory Committee will provide advice, suggestions, and evaluation of projects and results. The Committee will meet four or five times a year, as the occasion requires.

The following persons are members of the committee:

Friedrich A. Hayek, J.U.D., Dr. rer. pol., D.Sc., professor of social and moral science, University of Chicago. He was formerly director of the Austrian Institute of Economic Research; Tooke Professor of Economics, Science and Statistics, London; and Fellow of the British Academy and the Royal Economic Society. He is the author of *The Road to Serfdom, The Counter Revolution of Science,* and *Individualism and Economic Order.*

Felix M. Morley, A.B., B.A., Ph.D., D. Litt., LL.D. He is an editor, author, and foreign correspondent from Gibson Island, Md. He was a Rhodes Scholar at Oxford, a Hutchinson fellow of the London School of Economics, and a Guggenheim fellow. He was formerly a member of the staff of Brookings Institution and president of Haverford College and was awarded the Pulitzer prize for editorial writing. He is a fellow of the Royal Economic Society and was director of the Geneva office, League of Nations, and editor of the *Washington Post.* He is the author of *The Foreign Policy of the United States: Freedom and Federalism* and *The Power in the People.*

Herrell F. DeGraff, B.S., Ph.D., Babcock Professor of Food Economics, school of nutrition, Cornell University. He is a member of the American Farm Economic Association, the British Farm Economic Society, and the Canadian Farm Economic Society.

George C. S. Benson, A.B., A.M., Ph.D., president, Claremont Men's College, Claremont, Calif. He was formerly professor of public administration, Northwestern University; personnel director, administrative division, Office of Price Administration; chief research consultant, Council of State Governments; and research director, United States Commission on Intergovernmental Relations.

Aldon S. Lang, A.B., A.M., Ph.D., dean, Hankamer School of Business, Baylor University, Waco, Texas. He was formerly professor of economics and business administration and is the author of *Salient Factors Sustaining Prosperity* and *The Dynamics of American Capitalism.*

James W. Wiggins, B.S., A.M., Ph.D., professor of sociology and chairman of the department of sociology and anthropology, Emory University, Atlanta, Ga. He is the author of *The School Unit in Modern Society* and *Language in Society.*

GOVERNMENT SERVICES

AIR FORCE

How to Behave in Outer Space.—A training course in how to eat and perform other bodily functions under conditions of weightlessness was completed in December at Edwards Air Force Base, California. The students were America's seven handpicked astronauts, one of whom may ultimately be the first human to enter outer space. The training for the astronauts was conducted by doctors and pilots of the Air Training Command's Aerospace Medical Center. Doctors of the center's school of aviation medicine, at Brooks Air Force Base, Texas, started investigating the phenomenon of weightlessness or zero gravity in 1949. At that time the thought that man might someday escape earth's gravitational field was still considered in the realm of science fiction.

Scientists recognized that a simple act like eating would become a problem with food and containers floating eerily in the air. Even more complex physiological effects were anticipated, but research was limited because of the earth's gravitational field. Early experiments were conducted in the elevators of skyscrapers and copper mines, but the most successful technique developed so far is flying an airplane through a flight maneuver known as a parabolic curve. Acting themselves as subjects, researchers at the school of aviation medicine have sustained periods of weightlessness up to a full minute while flying. The purpose of the course was to acquaint the men with weightlessness and to develop equipment which will eventually be used in space flights. The instructors were two doctors from the school of aviation medicine, Major Willard R. Hawkins and Capt. James A. Roman. These officers flew hundreds of weightless maneuvers while experimenting with many types of containers and foods and carefully noted their problems in performing the various tasks a space pilot might be called on to perform.

Each astronaut was taken aloft four times, and on each flight was put into zero gravity several times. All of the men are former test pilots, and have previously experienced weightlessness for short periods, but during these tests, riding as passengers, they were free of the requirement of flying the airplane and could spend their time learning to handle things, including the highly concentrated liquid and semiliquid foods especially designed for them. During the tests, the future spacemen were wired for the collection of a variety of physiological data. The foods and liquids were contained in plastic "squeeze-type" bottles and tubes, much like toothpaste tubes. The astronauts, eating while weightless, can either squeeze the nourishment into their mouths or draw the food from the tubes by suction.

NAVY

Reassignment.—Rear Adm. H. J. Van Peenen took over his new assignment as commanding officer of the U. S. Naval Hospital, Portsmouth, Va., relieving Capt. W. H. Schwartz, on Nov. 30. Formerly assigned as district medical officer of the Fifth Naval District, Rear Admiral Van Peenen will continue to serve in that capacity in addition to his assignment at the naval hospital.

MEDICAL NEWS

FLORIDA

Dr. Prystowsky Honored.—Dr. Harry Prystowsky, professor of obstetrics and gynecology, University of Florida College of Medicine, Gainesville, was presented with the Jayson, signifying his selection as one of the "Ten Outstanding Young Men" in the nation, Jan. 16 at the annual awards congress of the national Junior Chamber of Commerce in Hartford, Conn. He was the only physician included in the 1959 selections, although a colleague, Dr. Richard T. Smith, head professor of pediatrics at the University of Florida, was similarly honored last year. Dr. Prystowsky was selected for the honor "for his contributions as a physician, educator, and scientific investigator." A native of Charleston, S. C., Dr. Prystowsky graduated from the Medical College of the State of South Carolina. He later worked with Prof. D. H. Barron on fetal physiology at Yale University School of Medicine, New Haven, Conn. He was appointed head professor of obstetrics and gynecology at the University of Florida in 1958.

MASSACHUSETTS

Invite Applications for Research Award.—To honor the memory of the late Dr. John J. Larkin Jr., the Saint Luke Guild of Catholic Physicians makes available each year the John J. Larkin Jr., Memorial Grant in Aid for Medical Research. A sum of $1,000 is designated for this award. The grant may be awarded to a research fellow, teaching fellow, resident, intern, medical or premedical student who is a resident of the Greater Boston area. This award may be given to one individual or may be divided among several individuals who are working on the same project. In the event "no suitable applicant is received" the award may accumulate until the following year. Applicants should apply in writing to Dr. Howard J. Christian, Carney Hospital, 2100 Dorchester Ave., Dorchester, Mass. Applicants are requested to submit information regarding residence, academic and professional qualifications, and a detailed account of work accomplished or planned in the special field of investigation selected. This application should be accompanied by a letter from the director of the school or hospital department in which the work will be carried out. It is expected that publication of papers based on work aided by this grant will include the usual footnote acknowledging such support. Applications must be filed before March 15. The award will be announced about March 22.

MICHIGAN

Conference on Comparative Medicine.—The first annual Michigan Conference on Comparative Medicine will be held March 21-22 at the Kellogg Center for Continuing Education, Michigan State University, East Lansing. This conference is being sponsored jointly by the Michigan Department of Health, the University of Michigan Medical School, the Wayne State University College of Medicine, and the College of Veterinary Medicine at Michigan State University. Thirteen topics are scheduled with discussions to follow each presentation. Out-of-state participants will include the following: Dr. Jacob Furth, Boston; Dr. Ludwik Gross, Bronx, N. Y.; W. E. Heston, Ph.D., Bethesda, Md.; J. N. Ott, Winnetka, Ill.; Rosalie Peterson, R.N., Bethesda, Md.; and Charlotte Street, New York City. Dr. William L. Simpson, scientific director, Detroit Institute of Cancer Research, will speak at the banquet to be held 6:30 p. m., March 21. For information, write the Kellogg Center for Continuing Education, Michigan State University, East Lansing, Mich.

Report on Communicable Diseases.—The Michigan Department of Health reported that diphtheria and typhoid fever cases dropped to all-time lows in Michigan in 1959 but several other communicable diseases staged minor upsurges. Only three diphtheria cases were reported in Michigan last year. The previous low was six cases in 1958 and the all-time high was 12,075 in 1921. Typhoid fever caused only eight cases of illness in 1959, compared with the previous low of 12 cases in 1957 and the all-time high of 5,122 cases in 1900. For the 12th straight year, no smallpox cases were reported in Michigan in 1959. There were 7,086 cases in 1902. Whooping cough cases last year totaled 3,001, compared with the 1958 total of 1,233, which was the all-time low for Michigan. The all-time high was 16,512 cases in 1941. Hepatitis cases last year totaled 1,136, compared with 688 in 1958. The all-time high since the disease became reportable in 1945 was 1,419 cases in 1954 and the all-time low was 9 cases in 1948. Scarlet fever was up in 1959 to 9,452 cases, compared with 5,380 in 1958. The all-time high of 24,798 cases was recorded in 1937. Paralytic poliomyelitis accounted for 145 cases in 1959, compared with 557 in 1958 and the low since

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

vaccine became available of 121 cases in 1957. Tuberculosis dropped in 1959 to 5,045 cases, the second lowest 12-month total in the last 30 years. In 1957 there were 5,011 cases and in 1958, 5,658.

University News.—At the recent Central Divisional Meeting of the American Psychiatric Association held in Detroit, a plaque was awarded to the Wayne State University department of psychiatry and its main teaching and clinical facility, the department of psychiatry, Detroit Receiving Hospital, for "the best scientific exhibit presented at the meeting." This award was received from representatives of all the midwestern states. The exhibit was on the diagnosis, understanding, and treatment of emergency psychiatric problems.——The department of dermatology at the University of Michigan Medical Center has won the J. N. Taub International Memorial Award for Psoriasis Research which carries a $1,000 grant to the winners. The three-year-old memorial is administered by Baylor University, Texas. Selection of the University of Michigan was based on professional articles on psoriasis published by staff members during the past two years.

MINNESOTA

Surgeons Meeting in Minneapolis and Rochester.—A four-day sectional meeting of the American College of Surgeons will be held in Minneapolis, April 11-13, and in Rochester, April 14. Headquarters in Minneapolis will be Hotel Leamington, and in Rochester will be Mayo Clinic. Dr. Horace G. Scott, Minneapolis, chairman of the advisory committee on local arrangements, reports that a series of hospital programs will be presented in addition to sessions in the hotels. There will be a one-day otolaryngology program and a one-day ophthalmic surgery program in Rochester. A discussion on activities of the college will be held during the fellowship luncheon on Tuesday noon, and Dr. Isidor S. Ravdin, chairman, board of regents, and president-elect of the college, will preside. On April 12, Dr. Ravdin will be the major speaker at the college dinner. His topic will be "Some of the Problems of Residency Training." Panel discussions are planned on postoperative management of the problem amputee and pitfalls in biliary tract surgery. Symposiums are planned on trauma and cancer of the cervix. Dr. H. Prather Saunders, Associate Director, American College of Surgeons, 40 E. Erie St., Chicago 11, is in charge of all sectional meetings for the college.

MISSOURI

Plan Bank for Eye Tissue.—An agreement for the establishment of an eye tissue bank at the University of Missouri School of Medicine, Columbia, with financial support from the Lions Clubs of Missouri has been signed by the university and the Lions Clubs. The agreement had been previously approved by the University board of curators. The bank will be known as the "Lions Eye Tissue Bank of the University of Missouri." The agreement states that it is being set up "in recognition of the fact that the Lions Clubs of Missouri have a deep and enduring interest in a program for the aid of those who have visual difficulties amendable to medical treatment and that the University of Missouri and its School of Medicine has the interest, professional personnel and responsibility for the teaching and training of physicians in this field." Under terms of the agreement the School of Medicine will direct the operation of the bank in the receipt, processing, and distribution of eye tissue. The bank is expected to serve Missouri and adjacent area, especially to the west. An administrative advisory committee of representatives of the Lions Clubs of Missouri and of the university will be established. Dr. John A. Buesseler, associate professor and chief of ophthalmology at the University of Missouri, will be in charge of training in eye tissue preservation and transplantation methods.

NEW YORK

Groups Join to Improve Care of Aged.—The efforts of four major organizations in the field of health to improve the welfare of New York State's aged citizens have resulted in the formation on Nov. 24 of the New York State Joint Council to Improve the Health Care of Aged. The organizations are the Medical Society of the State of New York, the Dental Society of the State of New York, the New York State Hospital Association, and the New York State Nursing Homes Association. Their meeting to form the Joint Council was held at the headquarters of the State Medical Society. The council stated its objectives as follows:

The exchange of information on activities and plans of its members and other organizations in the field of the aging.
Coordination of related programs conducted by member organizations.
Development of jointly sponsored projects.
Public dissemination of information on health care of the aged.

Presiding at the meeting was Dr. Joseph J. Witt, of Utica, chairman of the subcommittee on aging and nursing homes of the medical society's committee on public health and education. Dr. Stephen A. Graczyk, Buffalo, is co-chairman of this subcommittee. Elected as officers of the New York State Joint Council were: Dr. Witt, chairman; Mr. A. E. Barlow, Canton, vice-chairman; Charles A. Wilkie, D.D.S., Brooklyn, executive secretary of the State Dental Society, secretary; and Dr. Martin Cherkasky, of the Bronx, member of the board of governors of the Greater New York Hospital Association, a component of the State Hospital Association, treasurer.

New York City

Physicians' Wives Plan Dinner Dance.—The Physicians Wives' League of Greater New York, which has been assisting indigent physicians and their families for more than three decades, will hold a Valentine's Day Dinner Dance on Sunday, Feb. 14, 6:30 p. m., at the Starlight Roof of the Waldorf-Astoria Hotel. Tickets are $15 per person, and reservations are obtainable from the Chairman, Mrs. Louis Wexler, 5 E. 76 St., New York City (LE 5-1682). All physicians, their wives, and friends are invited.

Teachers Complete Course in Ailment Detection.—Forty-three of the city's elementary, junior high, and high school teachers Jan. 12 completed a 15-week in-service course at the Hospital for Joint Diseases. The teachers were shown how to detect orthopedic ailments in their pupils and instructed in the handling of handicapped youngsters in the classroom. The course was sponsored jointly by the hospital and the Board of Education. Lecturers included physicians, nurses, social workers, and rehabilitation counselors. The course was first offered last spring and repeated in the fall term.

Doctors' Orchestra Gives Concert.—The Doctors' Orchestral Society of New York, of which Dr. Harvey Salomon is president and Mr. Norman Masonson conductor, presented a memorial concert on Dec. 13. Featured soloists were Miss Marilyn Dubow, violinist, and Mr. Robert Ward, guest conductor and former conductor of the group. The program included Mendelssohn's Violin Concerto in E Minor, Beethoven's Seventh Symphony, and Gabrielli's Sonata Pian' E Forte for Brass. Physicians, dentists, nurses, and members of allied professions are invited to become members of this organization which rehearses Thursday evenings at 8:30 p. m. in the auditorium of the Stuyvesant High School, 15th St., and First Ave., New York City. For details contact: Dr. Benjamin A. Rosenberg, 909 President St., Brooklyn 15 (NEvins 8-2370).

NORTH CAROLINA

Program in Medical Sociology.—A new training and research program to provide for effective collaboration between the social sciences and health fields was established at Duke University, Durham. The program is headed jointly by John C. McKinney, Ph.D., chairman of the Duke sociology department who has received the additional title of professor of medical sociology; and Dr. Ewald W. Busse, chairman of the Duke Medical Center's psychiatry department. Personnel holding joint appointments in the sociology and psychiatry department comprise the staff for the program. Drs. McKinney and Busse explained that the program was established "in recognition of the need for social scientists in medicine." The new program at Duke is concerned primarily with research that utilizes the combined knowledge and skills of specialists in the social sciences and in medical health fields. The other principal activities are teaching at the undergraduate level and training research investigators in medical sociology.

PENNSYLVANIA

Dietetic Meeting to Consider Feeding in Space.—The annual spring meeting of the Pennsylvania Dietetic Association will be held April 28-29 at the Penn Harris Hotel, Harrisburg. The theme will be "Setting our Sights for the Space Age." The program will feature a demonstration and illustrated lecture on food and nutrition research for space and military feeding. At the annual banquet (West Shore Country Club) a travelogue, "Our Forty-ninth and Fiftieth States," will be shown. For information, write Miss Dorothy K. Waller, Chairman, Program Committee, Division of Nutrition, Department of Health, P. O. Box 90, Harrisburg, Pa.

Philadelphia

Faculty Promotions.—Promotion of seven faculty members, including Dr. Arthur G. Pratt from associate professor to clinical professor of dermatology was announced by Dean William A. Sodeman of Jefferson Medical College. Other promotions included Dr. John S. Carson, from associate to assistant professor of clinical anesthesiology; Dr. Abraham Freedman, associate to assistant professor of psychiatry; Dr. John E. Mock, instructor to associate in psychiatry; Dr. August P. Ciell, instructor to associate in otolaryngology; Dr. Jose H. Amadeo, assistant to instructor in surgery; Dr. Werner K. Welz, assistant to instructor in psychiatry; and Dr. Irwin L. Stoloff, from assistant to instructor in medicine.

University News.—An "association" between the 135-year-old Jefferson Medical College of Philadelphia and the 12-year-old Lovelace Foundation for Medical Education and Research in Albuquerque, N. M., was announced. Dr. William A. Sodeman, dean of Jefferson Medical College, and Dr. Burgess L. Gordon, director of medical education at Lovelace Foundation, charted the "areas of association." Dr. Sodeman stated, "We . . . can exchange information on our research programs on which Jefferson expends nearly a million dollars a year. . . . Lovelace conducted a vital phase of the physical examinations of the seven men selected as astronauts by the National Aeronautics and Space Administration."

GENERAL

Rehabilitation Fellowship for Foreign Physician.—The award of a fellowship for advanced study in rehabilitation in the United States to a Sierra Leone physician and his wife, a nurse, under the joint auspices of the World Veterans Federation and the World Rehabilitation Fund was announced by Dr. Howard A. Rusk, New York City. Dr. and Mrs. H. M. Contah, of Freetown, Sierra Leone, in West Africa, will undertake their studies at the Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center. Dr. Rusk, director of the Institute of Physical Medicine and Rehabilitation, is also president of the World Rehabilitation Fund. Dr. and Mrs. Contah will begin their studies early in 1960 and will represent Sierra Leone at the eighth world congress of the International Society for the Welfare of Cripples, to be held in New York, Aug. 28-Sept. 2.

University Surgeons Meet.—The 21st annual meeting of the Society of University Surgeons will be held Feb. 11-13 at the University of Minnesota Medical Center, Minneapolis, under the presidency of Dr. Henry T. Randall, New York City. Twenty-two papers are scheduled for presentation on the program. A panel on surgical education will be presided over by Dr. J. Englebert Dunphy, Boston, and will include the following papers:

The Growth of Research in the Surgical Training Program, Dr. Henry N. Harkins, Seattle.

The Experience at Minnesota, Dr. Owen H. Wangensteen, Minneapolis.

The Use of State Mental Institutions in Surgical Training Program, Dr. John A. Schilling, Oklahoma City.

Comments on Mental and Corrective Institutions in Minnesota, Dr. Bernard Zimmermann, Minneapolis.

A dinner dance is planned for the evening of Feb. 11, and the annual formal dinner will be held Feb. 12. For information, write Dr. Bernard Zimmermann, University of Minnesota Hospitals, Minneapolis 14, Minn.

Symposium on Heart Disease in Philadelphia.—Congenital heart diseases will be the subject of Deborah Hospital's second International Symposium on Current Concepts in Medicine to be held April 28, 29, and 30, in the Bellevue Stratford Hotel, Philadelphia. Eight sessions have been planned during the three days, each closing with open discussions and a summary of the subject material. The symposium is open to all interested physicians. There is no registration fee. Topics will include the following: Pathogenetic Factors in Congenital Heart Disease, Definitive Diagnosis of Congenital Heart Disease, The Fate of the Child with Unrelieved Congenital Heart Disease, Surgical Tools, Special Surgical Considerations, Surgery of Congenital Heart Disease, and Management of the Cyanotic Newborn. The later topic will be considered in a panel discussion. "Fireside Conferences" will be held at 8 p. m., Thursday. For information, write Deborah Hospital, 901 Walnut St., Philadelphia 7.

Texas University Announces Medical Cruise.—The University of Texas Postgraduate School of Medicine announced plans for the annual Texas Medical Cruise to the Caribbean, May 6-19. Faculty for the 14-day cruise will be Dr. Alfred E. Leiser, clinical instructor in medicine, Baylor University College of Medicine, and clinical assistant professor of medicine, University of Texas Postgraduate School of Medicine, Houston; Dr. L. Maxwell Lockie, head of the department of therapeutics, University of Buffalo (N. Y.) School of Medicine; Dr. Jarrell E. Miller, clinical professor of radiology, University of Texas Southwestern Medical School, Dallas; and Dr. Fred M. Taylor, associate professor of pediatrics, Baylor University College of Medicine, Houston. The cruise will depart from New Orleans on May 6 and return to New Orleans on the 19th. Ports of call will include: Havana, Cap Hatien, Port-Au-Prince, Montego Bay, and Grand Cayman. The itinerary will allow 25 hours of category I teaching credit for physicians desiring AAGP credit. For information, write the University of Texas Postgraduate School of Medicine, Houston, Texas.

Social Health Association Alters Name.—The American Social Hygiene Association voted to become the American Social Health Association, Frank H. Heller, ASHA president, announced. A national voluntary health and welfare organization, the American Social Health Association works "to promote those conditions of living, environment, and personal conduct which best protect the family as a social institution." In 1953, ASHA launched a nation-wide program in family life education. Through it, the association assists schools and colleges to develop new courses and training programs which "better equip teachers to work with children and young people." ASHA also promotes family life programs among parents and community groups. In cooperation with the Association of State and Territorial Health Officers and the American Venereal Disease Association, ASHA annually collects and publishes a joint statement on national statistics and trends in venereal disease. Last year's statement pointed up the rising incidence of venereal disease among teenagers and the need for increased reporting by private physicians.

Two Researchers Receive Neuromuscular Awards.—Two Kenny Scholar awards for 1960, each for $35,000 and made by the Sister Kenny Foundation, went to Dr. Eduardo Eidelberg, assistant research anatomist at the University of California School of Medicine, Los Angeles, and Dr. Leonard S. Wolfe, medical research fellow at Maudsley Hospital, London, England. The awards are given on recommendation of the medical advisory committee of the Kenny Scholarship program. Dr. Eidelberg, a native of Lima, Peru, will direct most of his investigations on the role of gamma-aminobutyric acid

tion in a new directory of Blood Transfusion Facilities and Services to be issued by early spring. The first directory produced by the council covered the year 1956 and included 2,202 facilities which collect, process, distribute, or use whole blood. Technical and operating procedures of blood banks and hospital transfusion services as well as sources and usage of blood are to be recorded. Also included will be approvals, supervision, reciprocity exchange systems, and other services such as tissue storage banks. The Joint Blood Council is a nonprofit organization formed and supported by the American Association of Blood Banks, American Hospital Association, American Medical Association, American Red Cross, and the American Society of Clinical Pathologists. Its primary purpose is to "establish a national blood program in order to assure an adequate supply of blood and blood derivatives to the civilian and military population at all times of peace or emergency." The forthcoming directory will list hospitals using blood as well as hospital blood banks, Red Cross centers, and community blood banks which collect, process, and distribute it. For information, write the Joint Blood Council, Inc., 1832 M Street, N.W., Washington 6, D. C.

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CORRECTION

Oscillometric Arterial Circulatory Norms.—An error has appeared in the article entitled "Oscillometric Arterial Circulatory Norms," by Bror S. Troedsson, in THE JOURNAL, Jan. 9, pages 141-145. In the summary, on page 145, is a sentence which reads, 'The first norm is called the gangrene point and is expressed by an oscillometric index of zero at the instep, zero above the ankle, and 1.125 above the knee." The last part of this sentence should read, "0.125 above the knee."

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 26-27. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination*. Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

ALASKA:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARKANSAS:* *Examination and Reciprocity*. Little Rock, June 9-10 (tentative). Sec., Dr. Joe Verser, Harrisburg.

COLORADO:* *Reciprocity*. Denver, April 12. *Examination*. Denver, June 14-15. Sec., Dr. John B. Farley, 1612 Tremont Place, Denver 2.

CONNECTICUT:* *Regular. Examination*. Hartford, Mar. 8-10. Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven. *Homeopathic. Examination*. Derby, Mar. 8. Sec., Dr. Ronald A. Davis, 38 Elizabeth St., Dover.

DISTRICT OF COLUMBIA:* *Reciprocity*. Washington, March 14. *Examination*. Washington, June 13-14. Deputy Director, Mr. Paul Foley, Department of Occupations and Professions, 1740 Massachusetts Ave., N.W., Washington 6.

GEORGIA: *Examination and Reciprocity*. Atlanta, June. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

GUAM: *Subject to Call*. Act Sec., Dr. F. L. Conklin, Agana.

INDIANA: *Examination*. Indianapolis, June 22-24. *Reciprocity*. Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

MICHIGAN:* *Examination*. Ann Arbor and Detroit, June 6-8. Sec., Dr. E. C. Swanson, 118 Stevens T Mason Bldg., Lansing.

MISSISSIPPI: *Examination*. Jackson, June. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

MONTANA: *Examination and Reciprocity*. Helena, April 5. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEBRASKA:* *Examination*. Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: *Examination*. Concord. March 9-12. Sec., Dr. Edward W. Colby, 61 South Spring St., Concord.

NEW MEXICO:* *Examination and Reciprocity*. Santa Fe, May 16-17. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

NEW YORK: *Examination*. Albany, Buffalo, New York City, Rochester and Syracuse, June 28-July 1. Sec., Dr. Stiles D. Ezell, 23 S. Pearl Street, Albany.

OHIO: *Reciprocity*. Columbus, April 5 and June 17. *Examination*. Columbus, June 16-18. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

OKLAHOMA:* *Examination*. Oklahoma City, May 31-June 1. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

PUERTO RICO: *Examination*. San Juan, March 1-5. Sec., Dr. Herminio Mendez Herrera, Box 9156 Santurce.

TEXAS:* *Examination and Reciprocity*. Fort Worth, June 20-22. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination*. Salt Lake City, July 6-8. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

VIRGINIA: *Examination and Reciprocity*. Richmond, June 13-17. Address: Board of Medical Examiners, 631 First St. S.W., Roanoke.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination*. Little Rock, April 21-22. Sec., Dr. A. W. Ford, Department of Education, Education Bldg., Little Rock.

COLORADO: *Examination and Reciprocity*. Denver, March 2-3. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

CONNECTICUT: *Examination*. New Haven, Feb. 13. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

DISTRICT OF COLUMBIA: *Examination*. Washington, May 23-24. Deputy Director, Mr. Paul Foley, Department of Occupations and Professions, 1740 Massachusetts Ave., Washington 6.

KANSAS: *Examination*. Kansas City, June 10-12. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburgh.

MICHIGAN: *Examination*. Detroit and Ann Arbor, Feb. 12-13. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

MINNESOTA: *Examination*. Minneapolis, April 5-6. Sec., Dr. Raymond N. Bieter, 165 Millard Hall, University of Minnesota, Minneapolis.

OKLAHOMA: *Examination*. Oklahoma City, April 15-16. [illegible] Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Okla[illegible]

TEXAS: *Examination*. Austin, Houston, Galveston [illegible] bly Dallas, April 15-16. Sec., Dr. Corr[illegible] State Office Bldg., 201 East 14th St., Au[illegible]

WISCONSIN: *Examination*. Madison, April [illegible] June 4. Sec., Dr. W. H. Barber, 621 [illegible]

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GEORGIA. *Examination and Reciprocity.* Atlanta, June. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

GUAM: *Subject to Call.* Act Sec., Dr. F. L. Conklin, Agana.

INDIANA: *Examination.* Indianapolis, June 22-24. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

MICHIGAN:° *Examination.* Ann Arbor and Detroit, June 6-8. Sec., Dr. E. C. Swanson, 118 Stevens T Mason Bldg., Lansing.

MISSISSIPPI: *Examination.* Jackson, June. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

MONTANA: *Examination and Reciprocity.* Helena, April 5. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEBRASKA:° *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: *Examination.* Concord. March 9-12. Sec., Dr. Edward W. Colby, 61 South Spring St., Concord.

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MINNESOTA: *Examination.* Minneapolis, April 5-6. Sec., Dr. Raymond N. Bieter, 165 Millard Hall, University of Minnesota, Minneapolis.

OKLAHOMA: *Examination.* Oklahoma City, April 15-16. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

TEXAS: *Examination.* Austin, Houston, Galveston and possibly Dallas, April 15-16. Sec., Dr. Cornelia M. Smith, State Office Bldg., 201 East 14th St., Austin.

WISCONSIN: *Examination.* Madison, April 9. Milwaukee, June 4. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

°Basic Science Certificate required.

tion in a new directory of Blood Transfusion Facilities and Services to be issued by early spring. The first directory produced by the council covered the year 1956 and included 2,202 facilities which collect, process, distribute, or use whole blood. Technical and operating procedures of blood banks and hospital transfusion services as well as sources and usage of blood are to be recorded. Also included will be approvals, supervision, reciprocity exchange systems, and other services such as tissue storage banks. The Joint Blood Council is a nonprofit organization formed and supported by the American Association of Blood Banks, American Hospital Association, American Medical Association, American Red Cross, and the American Society of Clinical Pathologists. Its primary purpose is to "establish a national blood program in order to assure an adequate supply of blood and blood derivatives to the civilian and military population at all times of peace or emergency." The forthcoming directory will list hospitals using blood as well as hospital blood banks, Red Cross centers, and community blood banks which collect, process, and distribute it. For information, write the Joint Blood Council, Inc., 1832 M Street, N.W., Washington 6, D. C.

Program to Advance Postgraduate Education.—Merck Sharp & Dohme, Division of Merck & Company, West Point, Pa., announced a postgraduate program "to facilitate postgraduate medical education" which is planned and administered by physicians for physicians. At the request of physicians' organizations, the program will help provide scientists and clinicians to discuss subjects of special interest with them. Funds and facilities will be available to support research conferences to contribute to the solution of research problems of "exceptional importance." The program will make grants-in-aid available for the support of postgraduate education courses. Administrators may choose the subjects and speakers of the courses to be added to their curriculums. Physicians presenting reports of "exceptionally broad interest" at medical meetings will be invited to summarize them in specially produced, open-circuit telecasts. Kinescopes of televised medical meeting reports will be edited to produce compact films for showing at local meetings and will be supplemental to the company's medical film library. Reprints of "outstanding papers" will be presented under the auspices of the postgraduate program. The Merck Sharp & Dohme Seminar Report distributed to the profession for more than 20 years offers illustrated reviews and discussions of clinical problems, and the Merck Manual, a frequently revised compendium of medical knowledge, may be purchased on a nonprofit basis. For information, write Merck Sharp & Dohme Postgraduate Program, West Point, Pa.

Ten Honored for Medical Contributions.—Ten men of American medicine have been named to receive Distinguished Achievement Awards "for their exceptional contributions to world medical progress." The awards are made annually by *Modern Medicine,* international medical publication. The 1960 recipients were chosen by the editorial board of the publication from nominations during 1959 by deans of the nation's medical schools, leaders of medical organizations, and readers. Award winners are:

Dr. Walter L. Bierring, professor emeritus of medicine, University of Iowa and director of the Iowa Health Department of Gerontology, Heart and Chronic Disease.

Dr. Alfred Blalock, professor of surgery, Johns Hopkins University School of Medicine, Baltimore.

Edward Allen Boyden, Ph.D., professor emeritus of anatomy, University of Minnesota and resident professor of anatomy at the University of Washington.

Dr. Albert H. Coons, American Heart Association career investigator, Boston.

Dr. Irving S. Cooper, director, Institute of Neuromuscular Diseases and professor of research surgery, New York University.

Dr. L. Emmett Holt Jr., professor of pediatrics, New York University, and director of Bellevue Hospital pediatric service.

Elmer V. McCollum, Ph.D., professor emeritus of biochemistry, Johns Hopkins University, Baltimore.

Dr. James V. G. Neel, professor of internal medicine and chairman of the department of human gentics, University of Michigan Medical School.

Dr. Albert B. Sabin, professor of research pediatrics, University of Cincinnati, and chief of the division of infectious diseases at Children's Hospital Research Foundation.

Nathan W. Schock, Ph.D., physiologist at City Hospitals, Baltimore.

The 1960 recipients join 240 other award winners who have been cited by *Modern Medicine* since the award program was instituted more than 20 years ago.

Mercy Ship Sponsored by Medical Journal.—Houston, Texas, is getting ready to see its own medical ship steam out to primitive parts of the world on an errand of mercy. The floating hospital and clinic, due to leave on its first cruise sometime in the spring, is the S. S. Dorin, a 144-ton ex-yacht which will sail under the flag of its sponsor, *Orthopedics.* The Dorin "will bring medical and surgical help to out-of-the-way places as well as some of the more familiar spots, native villages and crowded cities, disaster and epidemic areas—anywhere that the purpose for which the program was created can be put to good use." The Dorin was donated for the project by Dr. Paul S. Williamson, medical director of Savage Laboratories, Inc., of Houston, who purchased it in 1957. Launched in 1945 as an Army station-keeping hospital ship, the Dorin did not see wartime service. It was mothballed until Dr. Williamson purchased it. The ship is 110 feet long with a beam of 20 feet. It is presently equipped with 18 bunks in private and semiprivate cabins and

has a library-study, a full-sized living room and four bathrooms, a 12x40 foot clear deck area and two galleys. The ship will specialize mostly in orthopedic work, although its staff will call upon other members of the medical profession as they are needed. The medical staff of about eight doctors with five or six assistants will work on a voluntary basis; none will be paid. Crew of the ship will consist of a captain, engineer, assistant engineer, deckhand, and cook. The Houston project will be $75,000 a year, with less annual cost after the first two years.

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*Basic Science Certificate required.

DEATHS

Adkinson, Royal Chase, Denver; Rush Medical College, Chicago, 1895; died in the Presbyterian Hospital Oct. 29, aged 87.

Alexander, Morris James Ⓜ Punta Gorda, Fla.; Tulane University of Louisiana School of Medicine, New Orleans, 1915; served during World War I; past-president and a founder of the Charlotte Hospital, where he died Oct. 28, aged 69.

Almer, Julius Robley Ⓜ New York City; New York Homeopathic Medical College and Flower Hospital, New York City, 1917; veteran of World War I; died in the Beth Israel Hospital Oct. 31, aged 66.

Amarantes, Albert Roland, South Dartmouth, Mass.; University of Vermont College of Medicine, Burlington, 1929; for many years practiced in New Bedford, where he was physician on the staff of the New Bedford Board of Public Welfare; served on the staff of St. Luke's Hospital in New Bedford, where he died Oct. 25, aged 54.

Baker, Frederick Reuel Ⓜ Colorado Springs, Colo.; Columbia University College of Physicians and Surgeons, New York City, 1903; formerly county physician and coroner; on the staffs of the Glockner-Penrose Hospital, Memorial Hospital, and St. Francis Hospital; died Oct. 31, aged 82.

Ballantyne, Lowyd Whitcombe R. Ⓜ Colonel, U. S. Air Force, retired, Hendersonville, N. C.; Syracuse University College of Medicine, 1913; served in the regular U. S. Army; formerly flight surgeon and commanding officer of the 1600th Medical Group at Westover AFB; at one time chief flight surgeon at Hickam Field; upon his retirement in 1951 was awarded the Legion of Merit; died Oct. 18, aged 72.

Barber, Frank Ⓜ Lima, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1907; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; veteran of World War I; for many years president of the Lima High School Board of Education; served on the medical staff of the Eastman Kodak Company in Rochester, N. Y.; on the staffs of the Strong Memorial-Rochester Municipal Hospitals and the Genesee Hospital in Rochester, N. Y., where he died Oct. 26, aged 76.

Barr, Harry Clarence, Cleveland; Cleveland Homeopathic Medical College, 1904; served on the staffs of the Huron Road and Grace hospitals; died in Ludlowville, N. Y., Oct. 24, aged 77.

Blaylock, Richard D. Ⓜ Jackson, Mo.; Barnes Medical College, St. Louis, 1903; served as mayor and on the school board; on the staff of the Southeast Missouri Hospital, Cape Girardeau, where he died Oct. 25, aged 87.

Blodgett, Jean Cathcart Graves, Louisville, Ky.; Columbia University College of Physicians and Surgeons, New York City, 1944; interned at the Lenox Hill Hospital and served a residency at the Bellevue Hospital in New York City; certified by the National Board of Medical Examiners; at one time on the faculty of the University of Louisville School of Medicine; died in the Norton Infirmary Oct. 26, aged 42.

Bohringer, George Adam Ⓜ Chicago; Chicago Medical School, 1921; died in the Mount Sinai Hospital Nov. 9, aged 65.

Bondurant, Alpheus J. Ⓜ Temple, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1916; member of the American College of Chest Physicians; formerly associated with U. S. Public Health Service; served on the staffs of various administration hospitals; veteran World Wars I and II; from 1947 to 1952 chief of tuberculosis at O'Reilly Veterans Administration Hospital in Springfield, Mo.; chief of tuberculosis at the Veterans Administration Center, where he died Nov. 2, aged 67.

Brown, Louis Sylvester Ⓜ Hillsboro, Ill.; Washington University School of Medicine, St. Louis, 1902; served on the staff of the Hillsboro Hospital; died Oct. 27, aged 84.

Burlingame, Henry Orville, Fort Worth, Texas; Eclectic Medical University, Kansas City, Mo., 1913; died Oct. 28, aged 70.

Caire, Arthur Anthony Jr. Ⓜ New Orleans; Vanderbilt University School of Medicine, Nashville, Tenn., 1919; on the faculty of Tulane University School of Medicine; served in various capacities at the Touro Infirmary, where in 1957 a portrait was presented as a tribute to his many years of service with the hospital; died Oct. 31, aged 63.

Ⓜ Indicates Member of the American Medical Association.

Cargill, Walter Hurt Ⓜ Atlanta, Ga.; Emory University School of Medicine, 1942; interned at the Grady Memorial Hospital, where he served a residency; formerly a fellow at the Duke Hospital in Durham, N. C.; specialist certified by the American Board of Internal Medicine; at one time on the faculty of his alma mater; veteran of World War II; associated with the Veterans Administration Hospital, Piedmont Hospital, Georgia Baptist Hospital, and the Crawford W. Long Hospital, where he died Oct. 26, aged 40.

Carter-Rosenhauch, Edmund Ⓜ New York City; Uniwersytet Jagiellonski Wydzial Lekarski, Cracow, Poland, 1906; on the staff of the Medical Arts Center Hospital; died Oct. 29, aged 77.

Cazan, George Martin, Blythe, Calif.; University of Louisville (Ky.) School of Medicine, 1939; interned at the City Hospital in Cleveland; served a residency at the Good Samaritan Hospital in Cincinnati and Louisville City Hospital; served during World War II; died Oct. 30, aged 45.

Cohen, Harry M., Miami Beach, Fla.; Long Island College of Medicine, Brooklyn, 1930; veteran of World War II; died Oct. 30, aged 52.

Creswell, George William Ⓜ Washington, D. C.; George Washington University School of Medicine, Washington, D. C., 1925; served on the faculty of his alma mater; in 1942 appointed a special consultant in the division of venereal diseases, U. S. Public Health Service; in 1943 secretary of the medical staff at George Washington University Hospital; died Nov. 1, aged 66.

Dansky, Abram Eugene Ⓜ Berkeley, Calif.; University of Nebraska College of Medicine, Omaha, 1945; interned at the Michael Reese Hospital in Chicago; served a residency at the Veterans Administration Hospital in Hines, Ill.; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; on the faculty of the University of California School of Medicine; from 1946 to 1948 associated with the U. S. Naval Reserve; consultant in psychiatry, Ernest V. Cowell Memorial Hospital; died in the Herrick Memorial Hospital Nov. 1, aged 39.

Dare, Gilbert DeWitt Ⓜ Plattsburgh, N. Y.; Jefferson Medical College of Philadelphia, 1897; veteran of World War I; member of the board of directors of the Physicians Hospital; died Oct. 26, aged 82.

Denholtz, Emanuel, Irvington, N. J.; Maryland Medical College, Baltimore, 1912; Medico-Chirurgical College of Philadelphia, 1913; served on the staff of the Irvington General Hospital, of which he was a founder; died in the Presbyterian Hospital, Newark, Nov. 13, aged 69.

Denning, James Stewart Ⓜ Pasco, Wash.; St. Louis University School of Medicine, 1951; member of the American Academy of General Practice; past-president of the Benton Franklin Counties Medical Society; veteran of World War II and later served in the Air Force Reserve; on the staff of Our Lady of Lourdes Hospital; died in the Virginia Mason Hospital, Seattle, Nov. 1, aged 37.

Dickson, Charles Scott Ⓜ Utica, N. Y.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1920; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; consultant, Marcy (N. Y.) State Hospital and the Ilion (N. Y.) General Hospital; on the staff of St. Luke's–Memorial Hospital Center, where he died Nov. 16, aged 64.

Didrickson, Fredolph G. Ⓜ Montrose, Colo.; Central Medical College of St. Joseph, Mo., 1903; on the staff of the Montrose Memorial Hospital; died Oct. 28, aged 79.

Douglass, Hal C. Ⓜ Fort Worth, Texas; Tulane University School of Medicine, New Orleans, 1923; member of the American Academy of General Practice; veteran of World Wars I and II, died Nov. 7, aged 59.

Ferguson, Eugene Hobart Ⓜ Kansas City, Mo.; Rush Medical College, Chicago, 1925; specialist certified by the American Board of Obstetrics and Gynecology; veteran of World War I; on the staffs of St. Mary's Hospital and the Trinity Lutheran Hospital, where he died Oct. 27, aged 62.

Ferguson, Robert Claudius, Arcadia, La.; Memphis (Tenn.) Hospital Medical College, 1904; served as parish coroner; died in Shreveport Nov. 2, aged 89.

Gibbons, John Martin Ⓜ Great Neck, N. Y.; University of Pennsylvania School of Medicine, Philadelphia, 1929; veteran of World War II; specialist certified by the American Board of Internal Medicine; formerly on the faculty of Cornell University Medical College, New York City; senior attending physician in medicine at the North Shore Hospital in Manhasset; died in the New York Hospital, New York City, Nov. 6, aged 55.

Glenn, John Walter Ⓜ New Bedford, Mass.; University of Pittsburgh School of Medicine, 1944; interned at the Pittsburgh Hospital, where he served a residency; served a residency at the Boston City Hospital; past-president of the New Bedford Medical Society; specialist certified by the American

Board of Surgery; served as an instructor in anatomy at his alma mater; captain in the U. S. Air Force, 1946-1947; consulting surgeon, Sassaquin Sanatorium; on the staff of St. Luke's Hospital; associated with the Union Hospital; died in St. Luke's Hospital Nov. 5, aged 39.

Gottstein, Werner K. Ⓜ Chicago; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1921; served a residency at the La Rabida Jackson Park Sanitarium, where he was on the staff; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served on the faculy of Northwestern University Medical School and the University of Illinois College of Medicine; consulting pediatrician at the Jackson Park Hospital; associated with the Presbyterian-St. Luke's Hospital, where he died Nov. 21, aged 65.

Granady, James Theophilis Wilcox Ⓜ New York City; Howard University College of Medicine, Washington, D. C., 1920; received a Selective Service Medal and Congressional Certificate of Merit for his work during World War II; consulting hematologist, on the staffs of the Harlem Hospital and the Mount Morris Park Hospital, where he died Nov. 11, aged 70.

Grau, Robert Kenneth Ⓜ St. Paul; State University of Iowa College of Medicine, Iowa City, 1933; veteran of World War II; member of the American Academy of General Practice and the American Association of Railway Surgeons; on the staffs of Midway, Children's, St. Luke's, and Bethesda hospitals; died Oct. 31, aged 50.

Green, Elbert Pierce Ⓜ Jacksonville, Ala.; University of Georgia Medical Department, Augusta, 1899; died Oct. 28, aged 85.

Greenleaf, James S., Savannah, Ga.; Atlanta Medical College, 1898; died Oct. 29, aged 83.

Greenwald, Jerome Jack Ⓜ Malverne, N. Y.; L.R.C.P., and L.R.C.S., Edinburgh, and L.R.F.P.&S. of Glasgow, Scotland, 1940; interned at the Israel Zion Hospital in Brooklyn, where he served a residency; served a residency at the Maimonides Hospital in Brooklyn; served on the faculty of State University of New York College of Medicine at New York City, Brooklyn; associated with the South Nassau Communities Hospital in Oceanside, the Kings County, Maimonides and Jewish Chronic Disease Hospital in Brooklyn; died in the Community Hospital in Glen Cove Nov. 17, aged 46.

Griswold, George Wayne, Roswell, N. M.; Baylor University College of Medicine, Dallas, 1915; specialist certified by the American Board of Otolaryngology; on the staffs of the Eastern New Mexico Medical Center and St. Mary's Hospital; died Oct. 23, aged 67.

Hanley, John Patrick Ⓜ Stafford Springs, Conn.; Cornell University Medical College, New York City, 1906; past-president of the Connecticut State Medical Society; past-president of the Tolland County Medical Society; examiner for the Selective Service during World War II; served as health officer; on the staff of the Johnson Memorial Hospital, where he died Nov. 2, aged 77.

Healy, Dennis Bartholomew, Furnace, Mass.; Kentucky School of Medicine, Louisville, 1904; for many years practiced in Flaxville, Mont.; died Oct. 22, aged 79.

Henson, Samuel Lafayette Ⓜ Benton, Ky.; Vanderbilt University College of Medicine, Nashville, Tenn., 1914; health officer for Calloway, Marshall, Livingston, and Lyon counties; formerly health officer of McCracken County; died in the Western Baptist Hospital, Paducah, Nov. 1, aged 71.

Hicks, Joseph Harkess, Gainesville, Fla.; University of the South Medical Department, Sewanee, Tenn., 1904; for many years practiced in Orange, Texas; veteran of World War I; died Oct. 23, aged 82.

Hirst, Ottis Grady Ⓜ Prescott, Ark.; University of Arkansas School of Medicine, Little Rock, 1918; served during World War II; died in the Sparks Memorial Hospital, Fort Smith, Oct. 30, aged 63.

Hoover, William Francis Ⓜ Jamestown, N. Y.; University of Michigan Medical School, Ann Arbor, 1924; fellow of the American Academy of Dermatology and Syphilology; veteran of World War II; died in the Veterans Administration Hospital, Buffalo, Nov. 3, aged 60.

Hume, Omer Forest Ⓜ Richmond, Ky.; University of Louisville School of Medicine, 1917; veteran of World War I; formerly member of the state senate; died in St. Joseph Infirmary, Louisville, Oct. 30, aged 67.

Jackson, Jerome M., New York City; Long Island College Hospital, Brooklyn, 1909; died in the North Shore Hospital in Manhasset, N. Y., Nov. 2, aged 73.

Jividen, Perry Augustus Ⓜ Rutland, Ohio; Starling Medical College, Columbus, 1902; died Oct. 31, aged 83.

Johnson, Paul Abel Gareth Ⓜ Kansas City, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1927; veteran of World War II; on the staffs of the Trinity Lutheran and Krestwoods hospitals; member and past-president of the staff of

St. Joseph Hospital; died in the University of Kansas Medical Center in Kansas City, Kan., Oct. 26, aged 56.

Kelly, William Aloysius, New York City; Laval University Faculty of Medicine, Quebec, Canada, 1942; consultant for the Workmen's Compensation Board; served on the staff of St. Clare's Hospital, where he died Oct. 21, aged 47.

Kerschner, Jeremiah E. ® Tiffin, Ohio; Ohio State University College of Medicine, Columbus, 1914; associated with the Tiffin State Hospital; served as an honorary member of the White Cross Hospital staff in Columbus; member of the American Academy of General Practice; died in the Mercy Hospital Oct. 2, aged 69.

Klein, Ursula Natalia ® Oklahoma City, Okla.; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1954; interned at the Menorah Medical Center in Kansas City, Mo.; served a residency at the Medical College of Virginia Hospital Division, Richmond; radiologist at Veterans Administration Hospital; died Oct. 31, aged 34.

Knight, Harold Fuller, Wolcott, N. Y.; Syracuse University College of Medicine, 1915; formerly practiced in Rochester, N. Y., where he was on the staff of the Genesee Hospital and where he died Oct. 22, aged 72.

Kolb, Allie Carl ® Little Rock, Ark.; University of Louisville (Ky.) School of Medicine, 1917; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association; at one time served as superintendent of the State Hospital; served on the faculty of the University of Arkansas School of Medicine; formerly associated with the Veterans Administration; associated with the Arkansas Baptist Hospital, where he died Oct. 30, aged 73.

Kulik, Max William ® New York City; Hamburgische Universität Medizinische Fakultät, Hamburg, Germany, 1924; interned at Peoples Hospital in Akron, Ohio; died Sept. 8, aged 61.

Leeper, James Avery ® Lenoir City, Tenn.; Tulane University School of Medicine, New Orleans, 1928; on the staff of the Charles H. Bacon Hospital in London; died Oct. 25, aged 54.

Leonard, Arthur James ® Saratoga Springs, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1903; honorary surgeon, Saratoga Hospital; died in the Albany (N. Y.) Hospital Oct. 21, aged 79.

McCalip, Hugh Long ® Yazoo City, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1914; veteran of World Wars I and II; on the courtesy staff, King's Daughters Hospital, where he died Oct. 31, aged 68.

McCurdy, John A. ® Wheeling, W. Va.; University of Cincinnati College of Medicine, 1928; on the staffs of the Ohio Valley General Hospital and Wheeling Hospital, where he died Nov. 4, aged 57.

McGuinn, William Benedict ® South Orange, N. J.; Long Island College of Medicine, Brooklyn, 1935; interned at the Kings County Hospital and Brooklyn State Hospital in Brooklyn, and the Westchester Square Hospital in New York City; medical director of the New Jersey Bell Telephone Company; member of the Industrial Medical Association; veteran of World War II; on the staffs of the Hospital Center and New Jersey Orthopaedic hospitals in Orange; died Oct. 28, aged 53.

Machacek, Gerald Frank, Long Island City, N. Y.; born Jan. 28, 1897; Columbia University College of Physicians and Surgeons, New York City, 1922; specialist certified by the American Board of Dermatology; member of the American Academy of Dermatology and Syphilology; for many years on the faculty of his alma mater; veteran of World War I; since 1926 on the staff of the Columbia–Presbyterian Medical Center; served as visiting physician at Willard Parker Hospital in New York City; author and co-author of several definitive publications on the histopathology of dermatologic diseases; died in the Roosevelt Hospital, New York City, where he was visiting consultant, Nov. 8, aged 62.

Mayfield, Claude, Long Beach, Calif.; Medical College of Indiana, Indianapolis, 1902; specialist certified by the American Board of Radiology; died in Seaside Memorial Hospital Aug. 30, aged 83.

Miller, John Abraham, Beaver, Okla.; Columbian Medical College, Kansas City, Mo., 1901; also a dentist; served on the school board; died in the Beaver County Memorial Hospital Oct. 20, aged 88.

Moore, Christopher C., Itta Bena, Miss.; University of Georgia Medical Department, Augusta, 1902; served as president of the First National Bank; formerly on the board of the Greenwood–Leflore Hospital in Greenwood, where he died Oct. 31, aged 77.

Myrick, Thomas Southall ® Muenster, Texas; University of Texas School of Medicine, Galveston, 1932; member of the American Academy of General Practice; past-president of the Cooke County Medical Society; for many years president of the Cooke County Tuberculosis Association; served as city health officer and on the city council; for many years president of the school board; for two years president of the Muenster Lions Club; director of the Muenster State Bank; affiliated with the Gainesville (Texas) Sanitarium; died Oct. 28, aged 55.

Board of Surgery; served as an instructor in anatomy at his alma mater; captain in the U. S. Air Force, 1946-1947; consulting surgeon, Sassaquin Sanatorium; on the staff of St. Luke's Hospital; associated with the Union Hospital; died in St. Luke's Hospital Nov. 5, aged 39.

Gottstein, Werner K. Ⓜ Chicago; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1921; served a residency at the La Rabida Jackson Park Sanitarium, where he was on the staff; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served on the facuty of Northwestern University Medical School and the University of Illinois College of Medicine; consulting pediatrician at the Jackson Park Hospital; associated with the Presbyterian-St. Luke's Hospital, where he died Nov. 21, aged 65.

Granady, James Theophilis Wilcox Ⓜ New York City; Howard University College of Medicine, Washington, D. C., 1920; received a Selective Service Medal and Congressional Certificate of Merit for his work during World War II; consulting hematologist, on the staffs of the Harlem Hospital and the Mount Morris Park Hospital, where he died Nov. 11, aged 70.

Grau, Robert Kenneth Ⓜ St. Paul; State University of Iowa College of Medicine, Iowa City, 1933; veteran of World War II; member of the American Academy of General Practice and the American Association of Railway Surgeons; on the staffs of Midway, Children's, St. Luke's, and Bethesda hospitals; died Oct. 31, aged 50.

Green, Elbert Pierce Ⓜ Jacksonville, Ala.; University of Georgia Medical Department, Augusta, 1899; died Oct. 28, aged 85.

Greenleaf, James S., Savannah, Ga.; Atlanta Mediical College, 1898; died Oct. 29, aged 83.

Greenwald, Jerome Jack Ⓜ Malverne, N. Y.; L.R.C.P., and L.R.C.S., Edinburgh, and L.R.F.P.&S. of Glasgow, Scotland, 1940; interned at the Israel Zion Hospital in Brooklyn, where he served a residency; served a residency at the Maimonides Hospital in Brooklyn; served on the faculty of State University of New York College of Medicine at New York City, Brooklyn; associated with the South Nassau Communities Hospital in Oceanside, the Kings County, Maimonides and Jewish Chronic Disease Hospital in Brooklyn; died in the Community Hospital in Glen Cove Nov. 17, aged 46.

Griswold, George Wayne, Roswell, N. M.; Baylor University College of Medicine, Dallas, 1915; specialist certified by the American Board of Otolaryngology; on the staffs of the Eastern Medical Center and St. Mary's Hospit 23, aged 67.

Hanley, John Patrick Ⓜ Stafford Spri Cornell University Medical College, Ne 1906; past-president of the Connecticut cal Society; past-president of the Tolla Medical Society; examiner for the Select during World War II; served as health the staff of the Johnson Memorial Hospi he died Nov. 2, aged 77.

Healy, Dennis Bartholomew, Furnace, M tucky School of Medicine, Louisville, 1 many years practiced in Flaxville, Mor Oct. 22, aged 79.

Henson, Samuel Lafayette Ⓜ Benton, Ky.; bilt University College of Medicine, Na Tenn., 1914; health officer for Calloway, M. Livingston, and Lyon counties; formerly officer of McCracken County; died in the W Baptist Hospital, Paducah, Nov. 1, aged 71.

Hicks, Joseph Harkess, Gainesville, Fla.; U sity of the South Medical Department, Sew Tenn., 1904; for many years practiced in Or Texas; veteran of World War I; died Oct. aged 82.

Hirst, Ottis Grady Ⓜ Prescott, Ark.; University Arkansas School of Medicine, Little Rock, 19 served during World War II; died in the Spa Memorial Hospital, Fort Smith, Oct. 30, aged

Hoover, William Francis Ⓜ Jamestown, N. Y.; Un versity of Michigan Medical School, Ann Arbo 1924; fellow of the American Academy of Derma tology and Syphilology; veteran of World War II died in the Veterans Administration Hospital Buffalo, Nov. 3, aged 60.

Hume, Omer Forest Ⓜ Richmond, Ky.; University of Louisville School of Medicine, 1917; veteran of World War I; formerly member of the state senate; died in St. Joseph Infirmary, Louisville, Oct. 30, aged 67.

Jackson, Jerome M., New York City; Long Island College Hospital, Brooklyn, 1909; died in the North Shore Hospital in Manhasset, N. Y., Nov. 2, aged 73.

Jividen, Perry Augustus Ⓜ Rutland, Ohio; Starling Medical College, Columbus, 1902; died Oct. 31, aged 83.

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Kolb, Allie Carl Ⓜ Little Rock, Ark.; University of Louisville (Ky.) School of Medicine, 1917; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association; at one time served as superintendent of the State Hospital; served on the faculty of the University of Arkansas School of Medicine; formerly associated with the Veterans Administration; associated with the Arkansas Baptist Hospital, where he died Oct. 30, aged 73.

Kulik, Max William Ⓜ New York City; Hamburgische Universität Medizinische Fakultät, Hamburg, Germany, 1924; interned at Peoples Hospital in Akron, Ohio; died Sept. 8, aged 61.

Leeper, James Avery Ⓜ Lenoir City, Tenn.; Tulane University School of Medicine, New Orleans, 1928; on the staff of the Charles H. Bacon Hospital in London; died Oct. 25, aged 54.

Leonard, Arthur James Ⓜ Saratoga Springs, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1903; honorary surgeon, Saratoga Hospital; died in the Albany (N. Y.) Hospital Oct. 21, aged 79.

McCalip, Hugh Long Ⓜ Yazoo City, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1914; veteran of World Wars I and II; on the courtesy staff, King's Daughters Hospital, where he died Oct. 31, aged 68.

McCurdy, John A. Ⓜ Wheeling, W. Va.; University of Cincinnati College of Medicine, 1928; on the staffs of the Ohio Valley General Hospital and Wheeling Hospital, where he died Nov. 4, aged 57.

McGuinn, William Benedict Ⓜ South Orange, N. J.; Long Island College of Medicine, Brooklyn, 1935; interned at the Kings County Hospital and Brooklyn State Hospital in Brooklyn, and the Westchester Square Hospital in New York City; medical director of the New Jersey Bell Telephone Company; member of the Industrial Medical Association; veteran of World War II; on the staffs of the Hospital Center and New Jersey Orthopaedic hospitals in Orange; died Oct. 28, aged 53.

Machacek, Gerald Frank, Long Island City, N. Y.; born Jan. 28, 1897; Columbia University College of Physicians and Surgeons, New York City, 1922; specialist certified by the American Board of Dermatology; member of the American Academy of Dermatology and Syphilology; for many years on the faculty of his alma mater; veteran of World War I; since 1926 on the staff of the Columbia-Presbyterian Medical Center; served as visiting physician at Willard Parker Hospital in New York City; author and co-author of several definitive publications on the histopathology of dermatologic diseases; died in the Roosevelt Hospital, New York City, where he was visiting consultant, Nov. 8, aged 62.

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Myrick, Thomas Southall Ⓜ Muenster, Texas; University of Texas School of Medicine, Galveston, 1932; member of the American Academy of General Practice; past-president of the Cooke County Medical Society; for many years president of the Cooke County Tuberculosis Association; served as city health officer and on the city council; for many years president of the school board; for two years president of the Muenster Lions Club; director of the Muenster State Bank; affiliated with the Gainesville (Texas) Sanitarium; died Oct. 28, aged 55.

Noe, Charles Fred Ⓜ Amana, Iowa; State University of Iowa College of Medicine, Iowa City, 1898; on the staffs of St. Luke's Hospital and the Mercy Hospital, Cedar Rapids, where he was past-president of the staff and where he died Nov. 3, aged 83.

Padgett, Hubbard Corbin Ⓜ Roanoke, Va.; Medical College of Virginia, Richmond, 1913; on the staff of the Shenandoah Hospital; died in the Roanoke Memorial Hospital Oct. 31, aged 71.

Petty, Carlisle Rigdon Ⓜ Louisville, Ky.; University of Louisville School of Medicine, 1917; veteran of World War I; served as vice-president of the Tennessee Valley Postgraduate Medical Assembly; member of the American Association for the Surgery *of Trauma; fellow of the American College of* Surgeons; for many years practiced in Lynch, where he was chairman of the school board; on the staffs of St. Anthony, Jewish, and Kentucky Baptist hospitals, and St. Joseph Infirmary; died in the Jewish Hospital Oct. 26, aged 65.

Preston, Perry Brower Ⓜ Newark, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1901; veteran of World War I; died Oct. 31, aged 79.

Qualls, Harley Winfield Ⓜ Memphis, Tenn.; Vanderbilt University School of Medicine, Nashville, 1912; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; past-president of the Memphis and *Shelby County Medical Society; served as president* and secretary of the state board of medical examiners; on the staffs of the LeBonheur, Baptist Memorial, Memphis Eye, Ear, Nose and Throat, and St. Joseph's hospitals, and the Methodist Hos*pital, where he died Oct. 28*, aged 74.

Quillian, Willard Earl Ⓜ Neptune Beach, Fla.; Atlanta College of Physicians and Surgeons, 1900; veteran of World War I; for many years practiced in Atlanta, Ga., where he was on the faculty of Atlanta School of Medicine, vice-president and president of the board of health, a charter member of the staff of Emory University Hospital, and past-president of the International Civitan Club; died in Norwalk, Conn., Nov. 5, aged 83.

Royce, Emery Emmerson, Sparland, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1898; served on the staffs of the Proctor and St. Francis hospitals in Peoria; director of the Henry (Ill.) State Bank, of which he was formerly *president; for many years president of the school* board; died Oct. 27, aged 87.

Royster, Hubert A. Ⓜ Raleigh, N. C.; born in Raleigh Nov. 9, 1871; University of Pennsylvania Department of Medicine, Philadelphia, 1894; professor of surgery emeritus at the University of North Carolina School of Medicine in Chapel Hill, where a portrait was presented in 1953; dean and professor of gynecology, University of North Carolina Medical Department, Raleigh, from 1902 to 1910; later professor of surgery at Wake Forest College, now known as the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem; secretary of the state board of medical examiners for many years; past-president of the Raleigh Academy of Medicine, Tri-State Medical Association, Wake County Medical Society, state medical society, and Southern Surgical Association, of which he was for many years secretary; member of the American Surgical Association; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons, of which he was one of the founders; chairman of the Section on Surgery, General and Abdominal, of the American Medical Association, 1931-1932; *served as consulting surgeon for the North Carolina* Hospital for the Insane at Dix Hill, where a building was named in his honor; one of the founders and chief of surgical service at St. Agnes Hospital; served as chief of the surgical service at Rex Hospital; author of three books; died Nov. 7, aged 87.

Sherman, Calvin Weed, Clyde, N. Y.; Syracuse University College of Medicine, 1914; at one time president of the Clyde High School Board of Education, *school physician, health officer, and coroner;* died Oct. 26, aged 70.

Shoemaker, Abram J., Columbus, Ohio; Starling-Ohio Medical College, Columbus, 1909; member of the American Academy of General Practice; associated with the Grant Hospital, where he died Oct. 25, aged 75.

Skeel, Blandina Kern, Cincinnati; Northwestern University Woman's Medical School, Chicago, 1898; for many years practiced in Cleveland; died Oct. 25, aged 84.

Sloan, Henry Lee Sr. Ⓜ Charlotte, N. C.; born in Ingold, Aug. 6, 1886; University of Pennsylvania School of Medicine, Philadelphia, 1911; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; past-president of the Mecklenburg County Medical Society; served as chief of staff, Charlotte Eye, Ear and Throat Hospital, where he was one of the founders; on the staff of the Presbyterian Hospital; consultant, Charlotte Memorial Hospital; on the board of directors of First Union National Bank; died Nov. 5, aged 73.

FOREIGN LETTERS

AUSTRIA

Portal Hypertension in Childhood.—At the meeting of the Society of Physicians in Vienna on Nov. 20, M. Wenzl stated that only the so-called shunt operation can achieve a decompression of the pressure in the portal vein and prevent further hemorrhages in children with portal hypertension. This operation in children offers particular problems. Besides the fact that portal hypertension occurring in children, unlike that in adults, depends more frequently on extrahepatic processes, there are the specific anatomic characteristics of children. Decompression of the pressure in the portal vein can be obtained in children only by a broad portacaval anastomosis. Splenorenal anastomoses may easily become thrombosed and should, therefore, be avoided. For these reasons, the knowledge of the anatomic situation in the area of the portal vein is essential when a portacaval anastomosis is planned in a child.

Splenoportography may reveal whether or not the portal vein is occluded. In two patients the portal vein was varicosed and a side-to-side anastomosis was performed. In one of these the portal hypertension was associated with cirrhosis of the liver. In an additional patient, who also had cirrhosis of the liver, an end-to-side anastomosis was possible. In all these patients the greatly increased preoperative portal blood pressure was restored to normal after the operation. The operation should be performed early, since repeated hemorrhages may increase the operative risk.

E. Deimer reported that certain risks are associated with percutaneous splenoportography. These have, in general, limited the use of this highly informative procedure. An intrasplenic epinephrine test was performed on 120 patients, with the aid of laparoscopic and splenoportographic control, which made it possible to select those suitable for splenoportography. Puncture of the spleen was performed, an intrasplenic injection of 0.1 mg. of epinephrine was given, and the peripheral blood pressure was read at short intervals. Normally the intrasplenically injected epinephrine is removed by the liver and does not result in significant changes of the peripheral blood pressure, but in portacaval short-cut communications with hepatofugal blood flow, the epinephrine immediately reaches the greater circulation and is manifested by a rapid and marked increase in blood pressure. This test may also be used in the study of intestinal hemorrhages of doubtful origin. If the intrasplenic injection of epinephrine does not cause any essential increase in blood pressure, the possibility of varices must be excluded, while an increase in blood pressure suggests the presence of varices. The test is free of risk, since the epinephrine exerts its effect where it does not influence the bleeding. In patients with hemorrhage caused by varices, the epinephrine is carried so rapidly into the peripheral circulation that the portal pressure is not changed significantly. In patients with hemorrhage caused by peptic ulcers, the epinephrine is removed by the portal system before it exerts an effect on the systemic circulation.

CANADA

Health Service for Saskatchewan.—Now that a province-wide hospital insurance scheme has been launched in 9 of the 10 Canadian provinces, prophets have been predicting that provincial governments would not be long in taking the next step toward a general health insurance scheme to cover all medical care. Their prophecies were supported by recent events in Saskatchewan, which has for many years shown left-wing tendencies and which the government is socialist. A provincial election is due in 1960 and the premier of the province, Mr. T. C. Douglas, has made a campaign promise to provide a universal medical care service if he is reelected. Not to be outdone, the liberal leader has also made a statement to the effect that, if elected, he will hold a plebiscite to determine whether the public really wants a universal medical care program. Details of Mr. Douglas' proposed program are not known, but it is believed that it will be province-wide and compulsory, possibly with payment to physicians on a fee-for-service basis at a percentage of the schedule of fees of the College of Physicians and Surgeons of Saskatchewan. It is likely that funds would be raised by a sales tax and a small personal or family premium and that the program would go into operation in 1961.

The College of Physicians and Surgeons of the province is opposed to this plan because of its compulsory features, and on Oct. 21 a resolution was adopted by the College which affirmed that medical care has always been readily available to the public, regardless of its ability to pay, and that standards of medical service will deteriorate under

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The items in these letters are contributed by regular correspondents in the various foreign countries.

a government-regulated system. The doctors believe that there are other more urgent problems than this, such as the provision of better facilities for the mentally ill, the aged, and the convalescent and of more hospital and rehabilitative facilities.

A few days after the College meeting, the Saskatchewan Federation of Labor called on the government to inaugurate a complete medical care program which would include preventive and diagnostic as well as curative and rehabilitative services. The College of Physicians and Surgeons announced that its opposition was aimed directly at the compulsory feature, since the medical profession of Saskatchewan had itself organized and sponsored voluntary plans now embracing 33% of the population. The Labor Council of Regina, one of the two largest cities in Saskatchewan, then made a statement claiming that doctors could never achieve universal coverage, nor could their plan ever be fully comprehensive. They said that voluntary plans have proved costly since they are based on a constantly rising and uncontrolled fee schedule. Because of the cost, those in direct need of medical care, such as the unemployed, underprivileged, chronically ill, and underpaid, could not be covered by the voluntary plans.

Progress in Hospital Insurance.—Of the 10 Canadian provinces 9 have now been operating a government hospital insurance plan for periods varying from a few months to 11 years. A cross-Canada survey showed that hospital insurance has been put into effect in most provinces without bringing about a major crisis in hospital accommodation. The 10th province, Quebec, which was at first hostile to a federal-provincial insurance plan, is studying its hospital space with a view to entering the plan. Although some increase in general hospital crowding has been noted, it is difficult to say whether this is due to population increase, the introduction of hospital insurance, or a combination of both factors. There has been little or no public opposition to the principle of insurance against hospital bills, and such objections as have arisen have been connected with the method of financing, which varies from special taxes to monthly premiums. Thus retailers in one province complain about collecting the special taxes levied, and in another province the public fears that not all of the funds raised by a sales tax are going into the hospital plan.

Health Insurance.—In a series of addresses at the Annual Meetings of Provincial Medical Associations Dr. E. K. Lyon dealt with the question of government intervention in medical practice. He recalled that in 1949, the Council of the C. M. A. went on record as approving the prepayment of defraying the cost of illness, at which time they had insured about 8% of the Canadian population in medically sponsored plans, while the commercial insurance carriers had insured another 8%. Ten years later the medically sponsored prepaid plans have insured about 24% of the population and the commercial carriers have kept pace with this. Thus in 1959, 48% of the total population is covered by some type of health insurance.

In spite of this increase in popularity of medically sponsored health insurance programs, some members of the medical profession have opposed these plans. It has often been suggested that the medical profession should get out of the business of health insurance, scrap the work of the past 10 years, and leave the problem to the commercial insurance carriers or the government. In Dr. Lyon's opinion, this is the surest way of encouraging government intervention. The speaker also suggested that it was open to question whether in all circumstances the fee-for-service principle could be defended as the only way in which the medical profession could be remunerated for its services. This principle could possibly mean that the doctor who was physically capable of performing the greatest number of services, although not necessarily the best, would receive the highest pay and that many of the new and complicated procedures requiring teamwork could scarcely be paid for on other than a unit basis. He also believed that a change in the system of paying teachers of medicine was needed, since it was increasingly difficult for clinicians to devote half their time to teaching and make a decent living on a fee-for-service basis during the rest of the day. At present 20 to 25% of the medical population of Canada has chosen to earn its livelihood by other than fee-for-service practice.

Although the government can never render the necessary medical care to the people without the cooperation of the medical profession, the profession cannot render the necessary care without a large measure of government support. The reason Canada has not had direct governmental intervention in the personal liberty of the profession is that the profession and the government have been willing to sit down together and discuss medical-economic problems. The medical profession must continue to stand ready to consider all proposals genuinely designed to improve the health of the people.

Charity Funds.—The Central Council of Ottawa Service Clubs released a controversial and hard-hitting report on charity drives. Two of the main recommendations are likely to meet with strong opposition. The first is that the various voluntary health organizations be merged into one organization making one annual appeal for funds. It is suggested that distribution of funds raised for health purposes is now so poorly coordinated that, while large sums have been raised by various health societies, an appeal for the Institute of Experimental Medicine and Surgery in the University of Montreal was so inadequately supported that 80% of the budget came from United States sources. Many of the 197 voluntary health agencies in the United States are represented in Canada. Some of these organizations have raised more money than they know how to spend.

The second feature in the report which is likely to arouse opposition is the suggestion that the provinces enact legislation for the establishment of municipal commissions for the licensing and control of all charitable and religious appeals. The report also suggested that provincial and federal governments tighten their regulations for granting charters to charitable organizations, because, whether intended or not, charters signify to the mind of the public a measure of approval.

Legal Relationships Between Surgeon and Anesthetist.—Many physicians are confused about the legal relationships and responsibilities of surgeon and anesthetist in the operating room. An anesthetist and a lawyer have clarified this relationship (*Canad. Anaesthetists' Soc. J.* 6:299, 1959). Until 1942, when a precedent was set in Ontario, the surgeon was considered to have full charge in the operating room. The legal relationship between surgeon and anesthetist was then that of master and servant. In a case in which the anesthetist is a nurse, this situation might obtain, but since the preferred practice is now to use a medically qualified anesthetist, this view is held to be fallacious. The idea of the anesthetist as the surgeon's legal servant may have arisen from the fact that (1) the anesthetist is historically a newcomer in the domain of surgery; (2) the patient has usually chosen his surgeon but not his anesthetist; (3) the patient is primarily interested in the surgical procedure and not the anesthetic; and (4) the surgeon may choose the anesthetist himself. In many larger hospitals, however, the surgeon does not choose the anesthetist and the fact that the latter has been given working privileges in the hospital constitutes reasonable grounds to assume that he is competent.

The authors stated that in general the widely held belief that there is a legal or contractual relationship between anesthetist and surgeon is incorrect. The surgeon and the anesthetist are not liable for each other's acts and omissions and their responsibilities are not inextricably bound together. There are no grounds for believing that there is, or ever was, a legal master-servant relationship between them. The notion that the surgeon delegates a duty with regard to anesthesia to the anesthetist is correct only when it applies to a nurse anesthetist.

Stein-Leventhal Syndrome.—Stein and Leventhal described a group of patients in whom amenorrhea and infertility were associated with bilateral polycystic ovaries. These patients also showed hirsutism. In a series of 45 patients with this syndrome Tompkins and co-workers (*Canad. M. A. J.* 81:714, 1959) found that hirsutism was associated with increased urinary 17-ketosteroid excretion, which suggested that the excessive hair growth was a result of increased androgen secretion. The 17-ketosteroid levels were also strikingly suppressed by prednisone in doses of 10 mg. a day in all patients, which suggested that the adrenals were the source of most of the androgen and that no functioning tumor was present. After discontinuing the administration of prednisone, the mean 17-ketosteroid concentration failed to return to its initial level during six months of observation. It appeared, therefore, that intermittent rather than continuous therapy would satisfactorily suppress androgen excretion. The menstrual pattern appeared to improve with prednisone therapy, but this was difficult to interpret since the natural course of the oligomenorrhea or infertility in these patients and the placebo effect were not known.

Thioridazine in Mental Syndromes.—Animal studies of a new phenothiazine, thioridazine (Mellaril), indicated that its effects were comparable to those of chlorpromazine without the side-effects of the latter. Azima and co-workers (*Canad. M. A. J.* 81:549, 1959) compared the effects of thioridazine with those of chlorpromazine and promazine in mental illness. They found that thioridazine is effective mainly in combating psychomotor hyperactivity and excitation. The activity of the drug was similar in most cases to that of chlorpromazine. The main difference was an absence of extrapyramidal and hepatic complications with the use of thioridazine.

Staphylococcic Infection in Hospital Nurseries.—Frappier-Davignon and co-workers (*Canad. M. A. J.* 81:531, 1959) conducted a field study of 26 hospitals in the province of Quebec to determine the prevalence of staphylococcic infections in the nurseries and the influence on those infections of bathing the infants, transferring the newborn infant out of and into the nursery, and intensifying the scrub technique of the staff. In 13 accredited hospitals in which 16,000 births were reported in 1956, there were 201 cases of staphylococcic infection, an average incidence of 1.25% (range 0 to 4.7%) in a period when epidemics were not prominent.

Results clearly showed that it made no difference whether the infants were or were not bathed (with soap and water, oil, hexachlorophene, or alcohol), provided the infants did not leave the nursery and provided that the nurses and aides washed their hands with soap or hexachlorophene before handling each infant. Mere dipping of the hands in a chloroxylenol solution was equivalent to not washing them. The incidence of infection in hospitals where all or some of the babies were transferred out of and into the nursery was between 1.5 and 1.92%. In contrast, in hospitals where babies were on no account taken out of the nursery, the incidence of infection was only 0.1%. It would seem that when infants are transferred out of and into the nursery, it is also preferable to bathe them if the personnel do not use a scrub technique.

GERMANY

Operability in Patients with Enlarged Prostate.—R. Hasche-Klünder (*Med. Klin.* 54:1164, 1959) stated that advanced age is no contraindication for prostatectomy. It is not the age of the patient but his general condition that should be the basis for deciding whether surgical procedures or conservative treatment with an indwelling catheter and hormone therapy should be undertaken. The author performed a prostatectomy on a series of 12 men who were over 80 years of age; four of these were over 85. Six of them had had indwelling catheters for over four years and four of them had permanent bladder fistulas. One died as a result of embolism and one as a result of severe, intractable vascular collapse. The chief danger was not in the operation itself but in the postoperative complications.

Transurethral prostatectomy with diathermy is recommended for small adenomas in patients over 90 years of age. For the debilitated patient with poor circulation extreme dilatation of the prostatic urethra remains as an alternative. This is a palliative operation and can, if necessary, be repeated. In all the 10 patients treated by this method the amount of residual urine was reduced to less than 50 ml. This opportunity of helping patients for whom prostatectomy is no longer suitable should not be overlooked. In the case of patients with advanced cerebral damage, conservative treatment with an indwelling catheter is preferred, in which case bilateral vasectomy is recommended to prevent epididymitis. In many patients vasectomy plus esotrogen therapy and temporary catheterization produced good results for a time.

Bronchial and Pulmonary Fistulas After Pneumonectomies.—H. W. M. Rauch (*Thoraxchirurgie* 7:59, 1959) stated that in a series of 429 patients on whom pneumonectomies were performed for tuberculosis, 44 developed fistulas and 16 died as a result. The incidence of this complication fell from 16.6% in the period between 1951 and 1954 to 4.7% between 1955 and 1957. In 1957 it was only 3.1%. The patients most frequently affected were those with internal fistulas, extensive destruction of lung tissue, and large cavities (20 to 38%); the least frequently affected were those with tuberculomas (3.1%). Bronchial fistulas occurred in 92.3% of the patients in whom there were tuberculous changes in the bronchial wall near the line of resection and in 4.6% of the patients in whom the bronchus was affected peripheral to the line of resection.

The state of the bronchus must be considered of prime importance in relation to the occurrence of postoperative bronchial fistulas. The frequency of the occurrence of this complication is also related to the extent of the resection undertaken. Most of the fistulas occurred after combined resections (removal of one lobe and a portion of another), particularly on the left side. The technique of resection and the method of closing the stump were of relatively slight importance compared with the following factors. Choosing the right time to operate, strict observation of the indications for operation, and careful attention to preoperative and postoperative treatment were most important. In contrast to the marked decrease in the incidence of bronchial fistulas over the past few years, the results of treatment of fistulas, once they have occurred, showed no real improvement, at least as far as the author's series was concerned. One promising method of treatment was a modified form of myoplasty after surgical narrowing of the remaining cavity. This method produced healing in over 60% of patients.

Chloroquine for Skin Diseases.—P. Zierz of Heidelberg (*Ärztl. Prax.* vol. 11, no. 9, 1959) treated with chloroquine 165 patients who had skin diseases. In at least 67% good results were obtained. In 20 of 26 patients with chronic erythemata, solar eczema, or rosacea, complete remission occurred within two or three weeks. In patients with acute erythema there were occasional successes. In four of eight patients with scleroderma good subjective and objective results were achieved, but in the localized form of scleroderma no effect was obtained. In skin conditions with severe itching (kraurosis vulvae, lipomelanic reticulosis, lichen simplex, lichen ruber planus, prurigo nodularis, and certain forms of erythroderma) chloroquine had a beneficial effect mainly by reason of its antipruritic action. Chronic erythemas and lichen simplex regressed in at least 50% of the patients, often after a relatively short period of treatment. In 11% there were mild side-effects, for the most part gastrointestinal disturbances. Apart from this, one case of urticaria occurred, one of depression, and one of epileptiform attacks. Interruption of treatment was rarely necessary. Neurohistological examination of diseased skin before and after treatment with chloroquine tended to show that the antipruritic properties were at least partly due to an inhibitory (vascular) effect on inflammation. This antiphlogistic effect was confirmed by the rat's paw test but to a lesser extent than with ACTH.

ISRAEL

Rabies Control.—W. Silberstein, head of the central laboratories of the government, reported that between 1948 and 1958 rabies was detected in 1,153 animals, 726 of which were dogs. Peaks occurred in 1948 and 1949 and from 1954 to 1956. The disease caused 23 human deaths in the decade reported on. Immediate local treatment of bite wounds with a 20% solution of tincture of green soap or cauterization with nitric acid is an important preventive measure. Patients with severe bites were given an injection of hyperimmune serum of high titer before the active immunization was started. The general control measures consisted mainly of the immunization of domestic dogs and the eradication of wild animals, especially dogs, cats, and jackals.

Hereditary Hemolytic Trait.—A. Szeinberg and Ch. Sheva of Tel Hashomer Government Hospital reported at a meeting of the Jewish Medical Association that they found a metabolic abnormality of erythrocytes in all patients with favism and hemolytic reactions due to drugs as well as in a large proportion of the members of their families. The abnormality was characterized by a reduced glutathione (GSH) blood level and its instability, decreased activity of glucose-6-phosphate dehydrogenase, a high aldolase level, and a low rate of incorporation of radioactive glycine into glutathione in vitro. This abnormality was detectable in the umbilical cord blood. On a large scale population survey practically no subjects with this abnormality were found among Ashkenazic Jews, while about 60% of the Jews from Kurdistan, 25% of those from Iraq or Persia, 5% of Yemenites and immigrants from Turkey, and 2% of North African Jews were affected. Similar findings were also observed among non-Ashkenazic Jews from Greece, Egypt, and Sudan and in a small percentage of Arabs from central Israel.

Genetic studies suggested that the abnormality was hereditary and probably transmitted by a sex-linked, incompletely dominant gene. The transient GSH instability of neonates appearing in the first hours of life differs from this condition, as it is not hereditary, nor is it racially determined. The glucose-6-phosphate dehydrogenase activity in bloods from such subjects was high. This GSH instability could be corrected in vitro by the addition of glucose or inosine to the blood. This enzymatic defect was not limited to the erythrocytes and was detected in such other tissue as platelets, leukocytes, and liver cells.

Anemia in Pregnancy.—M. Rachmilewitz and coworkers (*Harefuah* vol. 57, no. 4, 1959) found that in a series of 1,100 women examined immediately after delivery, 312 (28%) were anemic, i. e., their hemoglobin content was below 10 Gm.%. About 34% of the anemic women were suffering from hypochromic iron deficiency anemia with low serum iron and normal serum vitamin B_{12} levels. In 9% a pure macrocytic anemia was found, with low serum vitamin B_{12} and normal serum iron levels. In the remaining 57% of the anemic women the anemia was of a dimorphic type with both serum iron and serum vitamin B_{12} levels much below normal, indicating a double deficiency. In a limited number of anemic women (49) folic and folinic acid serum and blood levels were also determined, and 20 had low folic acid levels. This suggested that in many of these patients a triple deficiency was present.

These deficiencies seemed to be due to various factors. In the first place the possibility of utilization by the fetus of these substances, irrespective of the levels in the maternal blood, needed to be considered. This assumption was borne out by the high serum iron, serum vitamin B_{12}, and blood folic acid levels in the fetal as compared to the maternal blood. An additional factor was the nutritional state of these women. The nutritional survey conducted in the homes of a limited number of these anemic women showed their caloric intake to be extremely low and their food to be especially poor in animal protein. This finding together with the above-mentioned factors might account for the development of the deficiencies described here. Anemia of pregnancy is rapidly increasing, as shown by comparison of the figures obtained in a survey in 1955-1956 (11.2%) with that found in 1958 (28%).

Health, Education, and Welfare Policy.—In a report from the Social Research Institute of the government, I. Kanev reviewed the achievements of 1958. He stated that a country's productivity and security cannot be assured amid poverty and disease. On the other hand, social services cannot be built up in a weak economy. Israel has tried to develop her economy while simultaneously taking in a flood of destitute immigrants and providing them with jobs as well as social services. One index of the well-being of the population is employment. Despite the rise in population there has been a drop in unemployment from 17,700 in 1953 to 9,300, or only 1.4% of the employable population, in 1958. Now that the number of workdays per month for every laborer in emergency employment projects has been increased to 17, each should be able to subsist at a minimum level on his wage.

Evidence that immigrants to Israel have become integrated into the country's general social standard is supplied by life expectancy figures, which have risen steadily since the country became independent, despite mass immigration. In 1957 the figures stood at 71.4 years for women and 68 years for men, compared with 54.1 years for both men and women in 1927. Perhaps the most serious implication of this change, from the point of view of social security, is the rising proportion of oldsters in the population. In 1957 only 4.5% of all Israelis were aged 65 or more, but at the present rate of increase the proportion will have risen to 7% by 1970. Experts conclude that the retirement age must be raised, particularly for women, who are, at present, pensioned five years before men.

Between 1957 and 1958 the birth rate fell from 26 to 24 per 1,000, and with the mortality having declined from 6.2 to 5.6, the rate of natural increase was 18.4 per 1,000 in 1958, compared with 19.8 in 1957. It had thus fallen below the level of 1951, the peak immigration year, which had 32 births per 1,000 and a natural increase rate of 26.2; it fell below even the war year of 1948, with its characteristically low birth rate of 26.3 and a natural increase rate of 19.6. The infant mortality was cut from 33.3 to 30.9 per 1,000 births between 1957 and 1958. In the immigrant camps the infant mortality fell from 157 in 1950 to 40.3 in 1956, the national average being 35.5. Among non-Jews it fell from 95.8 in the period between 1944 and 1948 to 51.3 in 1958, far lower than that of any Arab country. Incidentally, the general mortality among the non-Jewish population fell from 16.8 per 1,000 in 1944-1948 to 7.8 in 1958. The birth rate, 48 per 1,000 in 1958, was among the highest in the world. This reflects the striking rise in the standards of health, education, and welfare of Israel's Arabs, 20% of whom are now members of Kupat Holim (the Labor Sick Fund).

Israel now produces 70% of its food. The average caloric intake is approaching 2,900 a day, which places Israel among the countries whose nutrition is adequate. At the same time, however, the nutritional gap between various sections of the population is wide. Slow progress in the hygiene of food production and distribution, along with poor sanitation, has resulted in a rise in the incidence of dysentery from 27.7 per 10,000 of population in 1957 to 34.3 in 1958. Although malaria has been eliminated and typhoid and tuberculosis are on the wane, intestinal diseases (other than typhoid) continue to plague the country. Now that 75% of the population is covered by voluntary health insurance plans, preparations are under way for implementing a compulsory insurance scheme, for which a detailed plan has been submitted to the government. This would constitute progress over voluntary insurance in the sense that (1) all employers would pay an equal share, (2) insurance would cover all types of illness, while the rights of members under the present schemes are subject to limitations of age and prior disability, and (3) certain standards would have to be enforced in all hospitals and clinics.

The shortage of hospital beds is serious. It is particularly acute in mental hospitals and the surgical and orthopedic wards of general hospitals. In some hospitals beds for gravely ill patients are put up in corridors and aisles. Other difficulties are presented by the cost of medical care, which has risen faster than the general cost of living, and by the difficulty of supplying doctors to outlying areas. The enormous rise in the number of accidents should arouse profound concern. Work accidents are increasing faster than the number of workers. They numbered 67 for every 1,000 employees in 1954-1955, and 75 in 1957-1958, but their seriousness has been decreasing.

UNITED KINGDOM

A New Agent for Débridement.—The presence of necrotic tissue in an open wound is an obstacle to healing and the early application of skin grafts. In addition to surgical removal, various enzymatic preparations have been used to digest the dead tissue. Rob and Singer used a protease extracted from fig latex (Decebrin, Debricin) (*Brit. M. J.* 2:1069, 1959). This is used as a lyophilized powder which is dissolved immediately before use in a vegetable gum with suitable preservatives and buffers. This protease has a highly specific lytic action on fibrin, denatured elastin, and denatured collagen, but it has no effect on living or even partially denatured tissues. The lesions requiring débridement ranged from traumatic necrosis to chronic ulceration and were found in all sites of the body. Size, etiology, degree of infection present, and total duration of each lesion were recorded to provide a background for the assessment of the value of treatment in each patient. The criterion for assessment of the usefulness of the preparation was taken to be the percentage of slough disappearance after five days of daily applications or, in the case of outpatients, the number of applications required to remove the necrotic tissue. The results were good in 18, fair in 8, and poor in 7 patients. Two of those in the last group did not give the treatment a fair trial. The best results were obtained when the lesions were moist.

The Health of Britain.—The Ministry of Health, (Report of the Ministry of Health for the Year 1958, part 2, 1959, Her Majesty's Stationery Office) reported that the birth rate, which has continued to rise since 1956, was 16.4 per 1,000 population in 1958 and that the expectation of life remained the same over the last five years. At one year of age the expectation was still 69 years for boys and 74 for girls. The total of 740,715 births in 1958 was the highest for 10 years, and the stillbirth rate of 21.5 per 1,000 was the lowest ever recorded. On the other hand, the incidence of neonatal mortality remained practically unchanged. Perinatal mortality dropped slightly. Over 11,000 infants failed to survive their birth by a month, and to this wastage must be added 16,000 registered stillbirths.

The number of persons in the population over 65 years of age continued to increase, and there were 118 over this age in every 1,000 population. Diseases of the circulatory system continued to take their toll of persons in this age group and accounted for over 33% of the total deaths. Neoplastic diseases were a cause of 17% of the total deaths. There was little sign of any halt in the rising number of deaths from cancer of the lung, although the rate of increase appeared to be slowing. In the over-50-year age group the ratio of deaths from this cause in men and women was 6.6:1.0. In 1958 an average of 262 people died daily from malignant disease, 54 of them, or nearly 20%, from cancer of the lung. By comparison, the number of deaths caused by motor vehicles was 15 a day and by tuberculosis 12. The number of deaths from leukemia has risen rapidly. From 1911 to 1920 this disease caused 400 deaths annually. For the past three years the average was 2,300.

Morbidity and mortality for nearly all infectious diseases fell. Although many areas have not had a single case for five years, diphtheria showed an increase, with eight deaths. The number of immunizations against diphtheria fell. This may have been due to the prominence given to poliomyelitis vaccine. The incidence of poliomyelitis was 4.4 per 100,000 population. There was again a fall in the proportion of cases in the 5-to-15-year age group and a rise in the group under 5 years of age. About 14,900 cases of food poisoning were reported, a decrease of 100 from 1957. Processed and made-up meats, meat pies, cold meat, and stews were the usual cause. Six cases were associated with imported canned meat.

Venereal disease continued to decline in incidence. The number of patients with early infectious syphilis attending clinics for the first time fell, although the decline was not uniform throughout the country. There was an appreciable increase in the Merseyside, Manchester, and Tyneside areas. New patients in the later stages of the disease and patients with congenital syphilis were also fewer, but gonorrhea showed a steep rise in both sexes, particularly in London and areas where immigrants were numerous. Although penicillin is a remedy, failures and relapses were common. Some patients who discontinued treatment after symptoms subsided were believed to harbor latent infection. Leprosy was found in 280 patients, all of whom had contracted the disease abroad.

Diseases of the respiratory system were still the commonest group of illnesses in the country. Roughly one million persons in Britain had respiratory symptoms which could be accounted for by the bronchitis-asthma-emphysema group of diseases, principally in men over the age of 40 years. Of these, 15,000 to 20,000 die in the winter months, and many more have increasing respiratory disability. Deaths from all forms of tuberculosis in 1948 numbered 21,993 (19,088 pulmonary). In 1958 the total was 4,480 (3,990 pulmonary). The improvement was greatest in the younger age groups. The peak mortality from respiratory diseases was reached in 1954; roentgenographic studies were made in 3,154,600 persons, with the result that 6,481 new cases of tuberculosis were discovered. This corresponded to 1.8 cases per 1,000 persons. The common cold was still responsible for more visits to the doctor than any other disease. Arthritis and rheumatism continued to rank second to bronchitis as a cause of incapacity.

Illness Due to Aviation Oil.—Drs. Honor Smith and J. M. Spalding went to Morocco at the request of the World Health Organization to help investigate a widespread outbreak of illness, which has been traced to the consumption of cooking oil adulterated with aviation oil. Nearly 10,000 persons became ill, and more than 6,000 suffered from paresis of the legs. The oil, originally intended for servicing turbo-jet engines, was sold as machine oil at surplus stores near Casablanca. This was used to adulterate olive oil or peanut oil, and the mixture was sold for use in cooking. Twenty-seven men were arrested in connection with this crime. Since the adulterated oil has been sold many patients have been hospitalized with paresis. Drs. Smith and Spalding stated that the paralysis was due to tri-ortho-cresyl phosphate poisoning. The synthetic aviation oil, which was made to withstand the high temperatures of turbo-jet engines, contained 3% of this compound. The amount ingested at any one time was not great, but as nearly all cooking in Morocco is done in oil, practically the whole local population suffered from this poisoning ("jake ginger paralysis").

Irradiation Sickness.—The most distressing side-effects associated with therapeutic irradiation are nausea and vomiting, which until recently were treated with pyridoxine, with variable results. Solan (*Brit. M. J.* 2:1068, 1959) reported that 57 patients were selected at random and given tablets of prochlorperazine, pyridoxine, or a placebo. If after 48 hours no relief was obtained, 10 mg., three times a day, of prochlorperazine was given in place of the unknown tablets. Of the 57 patients who were expected to suffer from side-effects due to irradiation, only 48 did so. Prochlorperazine was more effective than pyridoxine or the inert control tablet and in the dosage used was practically free from side-effects, such as marked drowsiness. Maximum benefit was obtained when prochlorperazine was given with the first exposure to irradiation, or at least as soon as possible after the onset of symptoms.

MISCELLANY

SANDFORD FLEMING AND THE BEGINNING OF STANDARD TIME

Robert I. Harris, M.B., F.R.C.S. (C.), Toronto

In THE JOURNAL, May 16, 1959, the item "Anniversary of Standard Time," in From Other Pages deserves amplification. The person chiefly responsible for the adoption of standard time was Sandford Fleming (later Sir Sandford Fleming) who was born in Kirkcaldy, Fifeshire, Scotland, in 1827. His father possessed mechanical skill and the son excelled in mathematics. At 18 years of age he migrated to Toronto, Canada, where he became associated with the Mechanics Institute. In 1849 he initiated and took a prominent part in founding the Canadian Institute. This later became the Royal Canadian Institute, and is still active under this title. His contribution to railroad construction and to the development of Canada is widely acknowledged. On retiring from his railroad activities he became Chancellor of Queens University in Kingston, Ontario, and continued to be active in the scientific and educational life of Canada until his death in 1915.

Sandford Fleming in 1860.

Meetings of Royal Canadian Institutes, 1878-1879

In the winter of 1878-1879 the meetings of the Canadian Institute were much occupied by discussions on "A Movement for Reforming the Time Systems of the World and Establishing a Prime Meridian as a Zero Common to All Nations." Interest in the problem was initiated by two papers read before the Institute by Sandford Fleming on "Time Reckoning" and "Longitude and Time Reckoning." These activities marked the beginning of the movement which led to world-wide establishment of standard time. In his two papers Sandford Fleming pointed out the urgent need for a revision of the methods of time reckoning for the purpose of eliminating gross difficulties in navigation, railway and telegraph operation, and astronomical observations.

Influenced by the arguments of Sandford Fleming on the benefits of a uniform system of time measurement around the world, the Canadian Institute, in 1879, took steps to bring the importance of this problem to the attention of the learned societies of Great Britain, Europe, and the United States. In the next few years this action resulted in discussion of the subject of universal or cosmic time before such bodies as the American Metrological Society (New York, 1880), the International Geographic Society (Venice, 1881), the American Society of Civil Engineers (Montreal, 1881, and Washington, 1882), the American Association for the Advancement of Science (Montreal, 1882), the Italian Geographical Society (Naples, 1883), and the International Geodetic Society (Rome, 1883). At the meeting of the International Geographic Society in Venice in 1881, it was recommended, on the motion of Sandford Fleming, that an international conference be held in Washington as soon as possible.

Time Difficulties in Operation of Railroads in North America

The American Metrological Society, meeting in New York in 1880, received a report from its Committee on Standard Time, of which the chairman was Cleveland Abbe. This report acknowledged the previous work of the Canadian Institute and then outlined the difficulties in the operation of railroads and telegraphs, arising from the existence of a great number of widely different local times. (Abbe states that 74 different local times existed across the United States and they bore no consistent relation to each other.) His report was concerned in part with the technical problem of transmitting time signals from one part of the country to another. The report stated that the numerous existing and unrelated local times would be better replaced by time zones progressing from one to another by a one-hour difference in time and 15 degrees difference in longitude. Since this seemed impractical at that moment, the recommendation of the committee was that absolute uniformity of time throughout the United States be adopted for use by railway and telegraph offices. This was to be known as railroad and telegraph time and it was to become legal throughout the United States after July 4, 1880. It was further recommended that this standard railroad and telegraph time be that of the meridian six hours west of Greenwich. (This passes very close to St. Louis, Mo.)

Cleveland Abbe was a professor and was on the staff of of the signals office in Washington. From the report of his committee on standard time it is evident that he appreciated the ultimate value of a world-wide system of uniform time reckoning but felt the urgent need was for immediate reform in time reckoning in the United States to relieve the confusion in operating railways and telegraphs. His recommendation that this be accomplished by a railway and telegraph time uniform throughout the whole of the United States was decidedly unusual. Some eminent scientists strongly opposed the idea of standard time, and for curious reasons. It is amusing to read the following comment from Prof. Simon Newcomb, Superintendent of the Nautical Almanac, in Washington in 1882. "A capital plan for the millennium. Too perfect for the present state of humanity. See no more reason for considering Europe in the matter than in considering the inhabitants of the planet Mars. No! we don't care for other nations; can't help them and they can't help us."

The proposal of the International Geographic Society (1881) to hold an international conference in Washington made progress slowly. The American Society of Engineers (1882) petitioned the Congress of the United States to strive for European concurrence on a prime meridian on which a time system could be based; if this failed, determination of a zero meridian for the use and guidance of the western continent was requested. About the same time the American Metrological Society adopted the similar procedure of an appeal to Congress. The result was that a joint resolution of the House of Representatives and of the Senate was passed authorizing the President of the United States to call an international conference to select a prime meridian and recommend its universal adoption for the reckoning of longitude and the regulation of time throughout the world. The International Geodetic Society meeting in Rome in 1883 supported the proposal for an international conference for the establishment of a zero meridian for longitude and time.

International Conference on Standard Time, Washington, 1884

The international conference met in Washington in 1884. It was composed of representatives of 25 "civilized" nations. After prolonged discussion, rendered necessary in part because of the difficulties of translation of addresses delivered in various languages, the conference adopted the three basic principles. These were essentially the proposals originally set forth by Sandford Fleming in his addresses to the Canadian Institute in 1878-1879. The following resolutions were adopted: 1. A prime meridian would pass through the center of the transit instrument at the observatory of Greenwich. 2. The universal day would be the mean solar day, to begin for all the world at midnight of the prime meridian (Greenwich). Each successive hour would begin at the solar passage of the meridian 15 degrees westward. 3. The hours would be counted from 0 to 24.

The first two of these resolutions have been widely adopted throughout the world. The third resolution is used only to a limited degree. It is interesting to record the concern manifested over the adoption of a prime meridian—not because of unsoundness of the principle but because national rivalries and jealousies made it difficult to select any fixed meridian. At one stage the 180th meridian from Greenwich was advocated because it passed through the Bering Strait and the Pacific Ocean and touched no land except the Kamchatka peninsula. Good sense finally prevailed and led the delegates to agree on the Greenwich meridian, which for 200 years had been used by many of the world's navigators and cartographers. But France abstained from voting on the prime meridian resolution because French navigators based their calculations on a meridian passing through Paris.

After several preliminary meetings, a convention of railway managers was held in Chicago in October, 1883, at which it was determined to adopt a uniform standard of hours for the operation of railroads through the United States. F. W. Allen was the secretary of this convention, and he played a prominent part in effecting the adoption of the change. This is the accomplishment which is recorded in the article in the *B. and O. Magazine* quoted in THE JOURNAL of May 16, 1959. This was not the introduction of standard time as is now universally understood. It was the introduction of time zones to railway operation in North America. The time zones were one-hour, 15-degree longitude zones based on Greenwich as a prime meridian, but there was no attempt to apply the principle to anything but the operation of railways in the United States.

Sandford Fleming's Contribution to Establishment of Standard Time

Sandford Fleming was not the first or the only person to conceive the importance of a prime meridian as the point from which all reckonings in space and time for the whole world could be made, nor was he the first to suggest that the world be divided into time zones, each of one hour of time and 15 degrees of longitude, progressing westward from a prime meridian. He was the originator of the idea that each day should be divided into 24 consecutive hours. His great accomplishment was the procedure he devised to accomplish the establishment of standard time—first, to convince the learned societies of the world of the merits of cosmic time based on a prime meridian; second, to organize an international conference of scientists consisting of five representatives from each of 25 countries, each national group appointed by its own government and responsible to its own government; third, to have the conference meet in North America where the problem of standard time for railways was more acute than anywhere else in the world, because the east to west distances were so great; fourth, to nurture the conference through the difficulties of language and the prickliness of nationalities to almost unanimous acceptance of the scientific principles; and fifth, to succeed through the 25 national delegations in influencing their respective governments to accept the proposals and implement them by legislation. It was a great accomplishment to influence 25 governments through the deliberations of a group of scientists so that they simultaneously enacted uniform legislation to a humanitarian end.

A plaque is attached to the building at 58 Richmond St., East, Toronto, in which Sandford Fleming read his historic paper in 1879. It was then the Canadian Institute Building in which they held their weekly meetings.

St. George St. at Bloor (5)

CORRESPONDENCE

BUDGETS OF MEDICAL SCHOOLS

To the Editor:—After reading Dr. Maurice Visscher's thoughtful article in THE JOURNAL, Nov. 14, 1959, page 1450, on "The Decline in Quality of Medical Teaching," I feel constrained to comment on some of his ideas.

Although I have not seen any actual figures, I believe it is safe to assume that the budgets of many, if not most, medical schools are becoming increasingly dependent on "soft" money. I believe further that most of this "soft" money comes from various branches of the federal government. About 400 years ago, Sir Thomas Gresham, an English financier, stated his famous law or theorem that bad money drives good money out of circulation. I believe that some of the disturbing trends noted by Dr. Visscher are a result of the operation of Gresham's law.

Various grants for research and training are not difficult to obtain at the present time. These grants are usually for a period of one year, with a "moral" commitment from the granting agency for extensions for two to four additional years, if the Congress of the United States appropriates sufficient funds. With this kind of assurance, or lack of it, one can readily understand the reluctance of an able young physician, who has a minimum of two mouths to feed, to accept a research or teaching appointment in a medical school, even if a fairly attractive salary should be offered (which is usually not the case).

The presence of huge sums of "soft" money may very well take some of the pressure off the schools to build up an adequate amount of "hard" money, with its guarantees of at least some measure of permanence in appointments. In order to fill positions, then, the schools frequently are forced to appoint such candidates as are available, with little regard for teaching or research talent. This, I maintain, is Gresham's law at work and is at least a partial explanation for the decline in the quality of medical teaching which Dr. Visscher has described.

At this point I should like to propose a remedy—a means whereby at least some of the "soft" money can be hardened. Most research and training grants include an item of "overhead." Presumably this overhead money is used to defray the costs of administration. If, as I believe, the grants themselves constitute a threat to the quality of teaching, it is not unreasonable to have the grants provide an antidote. This could be accomplished by putting all or a substantial part of the overhead money into an education fund which would be administered as an endowment. The income from this fund would be earmarked for providing more or better faculty salaries for permanent appointees. Admittedly, the amount of new "hard" money thus created would not be great immediately, but it could become an important factor in medical school budgets within 5 to 10 years. While I realize that some administrators in medical schools may find this plan distasteful, I believe that in time they, too, would benefit by it.

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New York 32.

ELECTROCARDIOGRAM OF PATIENT IN ANAPHYLACTIC SHOCK

To the Editor:—With regard to the article entitled "Electrocardiogram of Patient in Anaphylactic Shock," by Bernreiter, which appeared in The Journal, Aug. 1, 1959, page 1629, there seems to be no justification from the evidence presented for the statement ". . . the myocardium and the coronary circulation are capable of participating directly in anaphylaxis . . ." Even if one accepts the assumption that this 74-year-old patient's electrocardiogram was normal before he was given penicillin (and it is a pity that "no tracing before the occurrence of shock was available for comparison") the occurrence of sudden severe respiratory distress and quick collapse, with pulse and blood pressure unobtainable, could easily have accounted alone for the whole electrocardiographic sequence of events. One does not need to invoke anaphylaxis to explain it. The author apparently recognizes that "anoxia during the severe cardiovascular collapse in an elderly arteriosclerotic person" might have been the basis for the apparent cerebral injury the patient suffered. Why not accept the same basis for the electrocardiographic sequence? One can often see this sequence during anesthesia on those occasions when the oxygen supply is inadequate and carbon dioxide removal is deficient, such as when there is respiratory obstruction or circulatory collapse, or both. Perhaps all this means is that "the myocardium and the coronary circulation are capable of participating directly in" anesthesia and surgery.

Since there was no mention of the use of oxygen and ventilatory assistance in the emergency resuscitation of this patient, it came as no surprise to read of the patient's subsequent disorientation. The heart protested loudly, the brain more quietly. One even wonders whether it is safe to assume that the scheduled operation was canceled. The patient's "shock" could have been due simply to the pain of the injection, and the subsequent appearance of urticaria may have been the entire sum and substance of the anaphylactic reaction.

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COMBINED ESTROGEN-ANDROGEN THERAPY

To the Editor:—Differing points of view about the treatment of common disease syndromes are all too frequent in medical practice. These differences are well illustrated in the first two articles in The Journal, Nov. 21, 1959. The first paper is entitled, "Contemporary Therapy of the Menopausal Syndrome," by Kupperman and co-workers, and the second, "Prolonged Estrogen Therapy in Postmenopausal Women," by Wallach and Henneman. Kupperman and associates report superior results with combined estrogen-androgen therapy, whereas Wallach and Henneman found no advantage in such a combination in the long-term treatment of patients with osteoporosis. The latter workers reported an incidence of complications of only 5% in patients taking prolonged estrogen therapy.

In my experience, and that of many other clinicians, estrogen administered in the dosage range used by Wallach and Henneman is followed more frequently by complications. These side-reactions can be prevented by therapy of the menopausal syndrome and postmenopausal osteoporosis with small doses of estrogens combined with testosterone. Other pertinent indications for such combined treatment have been outlined by me in previous communications. Another more cogent reason has been reported by Toro and co-workers (*Proc. Soc. Exper. Biol. & Med.* 97:819 [April] 1958) who found, in a group of elderly patients, that treatment with testosterone as well as with combined estrogen and testosterone in moderate doses is followed by much more calcium retention than is therapy with estrogens. This is not surprising when one compares the anabolic properties of these steroids.

For long-range treatment of postmenopausal osteoporosis, it seems wise to avoid prolonged estrogen stimulation of the accessory sex organs, especially when satisfactory preparations for oral administration of combined estrogen and testosterone are now commercially available; but for long-term therapy, the dosage of these combined hormone preparations must be conservative, if all complications are to be prevented. It is perhaps better to err in giving too little rather than too much, especially when treatment is to be continued for many months or years. There is, unhappily, a universal tendency to prescribe the steroid hormones in the pharmacological rather than the physiological dosage range.

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LET US STAND UP AND BE COUNTED

To the Editor:—Sadly, our profession is being progressively placed on the defensive. It has become the whipping boy of politicians of various groups, career administrators, lay secretaries, and "experts" who supply statistical norms which are accepted wholly because of their attached labels. The habit of insulting us on the one hand and complimenting us on the other has been almost reflexly established. Through lectures, writings, and diagnoses of our defects and shortcomings, laymen of professional as well as nonprofessional, ancillary, and associated occupations are really formulating our policies, albeit indirectly. Furthermore, we aid the process by permitting ourselves to be judged not by our peers but by second-echelon medical men who do not have primary and direct responsibility for patient care; e.g., the occasional physician who fails to discern more than fixed-tissue diagnosis, being unwilling to become aware of the need for a corrective operation in extreme conditions of pathological physiology, with the consequent vicious circle of edema, hemorrhage (gross or by diapedesis), and varying degrees of collagen disease. As a result, to a large degree, come forth such destructive terms as "rape of the pelvis" appearing in ill-founded articles in the press for which inaccurate information has been supplied by some of these "holier-than-thou" persons.

Since our profession has been placed on the defensive, overreactions have resulted which may, in time, lead to the deterioration and ultimately to the demoralization of medicine, to the extreme detriment of the United States. Already a tangible effect is to be noted in the reduction in both numbers and quality of our medical school applicants. We are at fault, despite the fact that our patients are receiving the best medical care ever, day in and night out. Is it not incumbent on us to recover our balance, react normally, and take charge of our own destiny within the limits of good citizenship?

A good beginning would be to "make haste slowly" in accepting the various panaceas, taking time to really prove or disprove the new theories. We should also practice self-examination and appraisal more and criticism of our fellow medical men less. Let us stand on our true record. Let not medicine with its traditions be changed into a technical calling, without "heart."

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TETANUS-LIKE REACTIONS TO PROCHLORPERAZINE

To the Editor:—We have treated a patient who had a tetanus-like reaction similar to those described by Scime and Tallant in The Journal, Nov. 28, 1959, page 1813. The reaction was immediately recognized because three other patients with extrapyramidal disorders caused by triflupromazine and prochlorperazine had been seen in the service area of our 150-bed hospital in the past nine months.

The present patient, a 30-year-old woman, had acute tonsillitis, for which she was treated with triacetyloleandomycin. On admission she complained of tightness in her jaw. This progressed to overt but intermittent trismus. She came to our emergency department, where she displayed intermittent involuntary protrusion of the tongue, spasms of the sternocleidomastoid and trapezius muscles which required her to support her head with her hand, mask-like facies, and oculogyric crises. She also experienced abduction spasms of the jaw, sufficient to make one fearful of dislocation. She denied using any phenothiazine and none had been prescribed by her family physician, one of us (H. B. P.). When the patient's sister was questioned, it was learned that she had been using suppositories prescribed by another physician for her child for nausea. These were identified as 25-mg. prochlorperazine suppositories. The patient then confirmed taking two of these on the day prior to admission and one on the morning of admission.

She received 96 mg. of phenobarbital by hypodermic injection without striking improvement in the ensuing 45 minutes. She was then given 1 Gm. of methocarbamol by slow intravenous injection. Complete symptomatic relief ensued within five minutes. She was given two tablets of this drug every four hours; she complained of slight tightness in the jaw muscles in the next few hours, but thereafter she felt well. The methocarbamol administration was discontinued after two days. We are unaware of the previous use of methocarbamol in this type of disorder, but the success observed in the present case of severe skeletal muscle spasms merits its further trial.

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SIMPLE OR RADICAL MASTECTOMY

To the Editor:—I was surprised to find in The Journal, Oct. 31, 1959, page 1220, an excerpt from an article by Dr. T. C. Case entitled "Simple or Radical Mastectomy?" The excerpt states that there is no proof that radical mastectomy is superior to simple mastectomy and that the latter, with postoperative radiation, is the preferred treatment for patients with operable cancer of the breast. I disagree with this view. The comparison of survival rates cannot be expected to disclose the superiority of either method, and to recommend simple mastectomy as the preferred treatment is to disregard the occasional patient who can be cured by the radical but not by the simple method. The reasons for these views are given in an editorial, "The Remarkable Vision of Dr. Jones," published in *Surgery, Gynecology & Obstetrics,* November, 1959, page 634.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Fatal Cardiovascular and Respiratory Failure Associated With Tracheotomy. N. M. Greene. New England J. Med. 261:846-848 (Oct. 22) 1959 [Boston].

The author presents 5 cases of fatal cardiovascular and respiratory collapse which occurred immediately after tracheotomy. It is assumed that these were due to rapid reversal of preexisting respiratory acidosis. Patients who have elective or semielective tracheotomies for relief of respiratory obstruction should be followed with frequent blood-pressure recordings; if hypotension should develop, it should be treated by the Trendelenburg position and the intravenous administration of vasopressors. Oxygen should be used sparingly.

Clinical Aspect and Therapy of Temporal Arteritis. C. Kind. Schweiz. med. Wchnschr. 89:1104-1108 (Oct. 17) 1959 (In German) [Basel, Switzerland].

The author reports the case of a 71-year-old woman with temporal arteritis, who was admitted to the medical department of the district hospital in Wetzikon, Switzerland. The patient complained of headache, fatigue, anorexia, and loss of weight. There was tenderness of the entire head on pressure, and particularly of the occipital and temporal regions. The temporal arteries on both sides were visible, tortuous, and thickened. Pulsation was hardly perceptible in these arteries. The lower jaw was very sensitive to pressure; opening of the mouth caused pain, and so did moving the head or neck. The erythrocyte sedimentation rate was considerably increased, and the total plasma protein and albumin values were reduced, with a relative increase of the globulin fractions, particularly of the alpha fraction. The headache increased, and a reddish-blue swelling was observed over the left temporal artery 17 days after the patient's admission to hospital. The evening temperature rose to 38 C (100.4 F), and there was a night sweat. An exploratory excision of 2 small pieces of the involved left temporal artery was carried out, and microscopic examination of the specimens revealed occlusion of the lumen. Focal fibrinoid necrosis was observed on the border between the intima and the media. Loose spindle-cell granulation tissue was progressing toward the intima and through the media into the adventitia. A few giant cells of foreign body type were present. The temperature was restored to normal by prednisone therapy with 30 mg. of the drug given daily. The erythrocyte sedimentation rate also was restored to normal, and so were the plasma protein changes. Because of a history of attacks of squinting and clouded vision, an ophthalmological examination was performed, which, however, did not reveal any functional deficiency or papilledema.

The suspicion of temporal arteritis is raised when patients of advanced age show the following symptoms: headache, sudden disturbances of vision, progressive arterial obstruction associated with loss of weight, and considerably increased sedimentation rate. The necessity of early diagnosis is stressed; it can be established histologically after exploratory excision of an altered artery. In doubtful cases, even in patients with negative microscopic findings, a therapeutic trial with prednisone is indicated. Recent reports in the literature advocate exploratory excision of the involved artery for diagnostic purposes and for relief of headache; institution of prednisone therapy, with high doses of 50 to 75 mg. of the drug per day until restoration of erythrocyte sedimentation to normal, and maintenance treatment, with continued follow-up of the erythrocyte sedimentation rate; and continued anticoagulant therapy for months. These measures may prevent the previously dreaded ophthalmological and cerebral complications.

Oral Hemorrhage Secondary to the Use of Varidase Buccal Tablets (Streptokinase-Streptodornase) in Conjunction with Anticoagulant Therapy with Hedulin (Phenindione): Case Report. A. M. Benshoff Jr. West Virginia M. J. 55:397 (Nov.) 1959 [Charleston].

The patient, whose history is reported, had sustained a large hematoma of the calf muscle when he was attacked by a dog; the skin was not broken. The author prescribed streptokinase-streptodornase (Buccal Varidase), 1 Varidase tablet to be taken 4 times a day, to be held in the mouth in the buccal pouch and dissolved. Approximately 48 hours later the patient telephoned, stating that he was bleed-

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The place of publication of the periodical appears in brackets preceding each abstract.

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ing from the oral cavity, both under the tongue and in the cheeks. The Buccal Varidase was withdrawn immediately. The patient had a history of myocardial infarction, and at the time he sustained the aforementioned hematoma, he had been receiving anticoagulant therapy with phenindione (Hedulin) for more than a year, with a prothrombin time consistently running very close to 20% (that is, prothrombin time, 30 seconds; control, 15 seconds). The author believes that the oral hemorrhage was the result of the combined use of Buccal Varidase tablets and Hedulin anticogulant therapy. He wonders whether or not it is advisable in patients with phlebitis, who might be on anticoagulant therapy, to use any enzymatic treatment. He fears that under these circumstances internal bleeding might result, which may not be obvious.

Transplantation of Bone Marrow and Antineoplastic Treatment: Infusion of Autologous Bone Marrow for the Treatment of Bone Marrow Aplasia Which Follows Administration of Both High Doses of Therapeutic Irradiation and Chemotherapy: First Clinical Observations. E. Storti, U. Torelli and M. Lenzi. Minerva med. 50:2891-2897 (Sept. 15) 1959 (In Italian) [Turin, Italy].

Autologous bone marrow, collected and preserved before the irradiation, was reinfused in 2 patients, 60 and 56 years of age, with cancer, who were exposed to high therapeutic irradiation. One patient received, in addition, a course of chemotherapy. The purpose was to repopulate bone marrow depressed by antineoplastic treatment. The first patient had a large tumor in the mediastinum and one in the abdomen; the second had a large bronchial carcinoma. The infusion procedure consisted of aspiration of 40 cc. of marrow from the posterior iliac crest of each patient, which was rinsed with heparin, 1,000 units per milliliter. The marrow was placed in 4 sterile tubes, each containing 10 ml. of 30% glycerol in Tyrode's solution, and was preserved at a temperature of —79 C according to the modified method of Barnes and Loutit.

The first patient received a course of irradiation therapy for 60 days; the total dose to the irradiated area of the chest was 12.88 megagram-r and to the abdomen, 27.17 megagram-r. The total irradiation dosage of the second patient was 4,250 r for 21 days. This patient also received a course of chemotherapy, consisting of the intravenous administration of triethylene thiophosphoramide in daily doses of 10 mg. for 20 days. The antineoplastic therapy produced improvement of the malignant picture in the mediastinum of the first patient and in the bronchi of the second, along with amelioration of the general state of both patients. The reinfused marrow corrected fully the hematopoietic depression in both patients within a month of the reinfusion. The authors believe that the good results obtained in these 2 patients warrant further application of this procedure.

Cardiopulmonary Function in Pulmonary Fibrosis. L. R. Zohman and M. H. Williams, Jr. Am. Rev. Resp. Dis. 80:700-704 (Nov.) 1959 [New York].

The authors performed cardiopulmonary function studies on 47 adult patients with roentgenographic evidence of pulmonary fibrosis. Diagnoses included tuberculosis, sarcoidosis, silicosis, and fibrosis of unknown causation. Seventy-two measurements of vital capacity and of diffusing capacity during exercise were made in these patients. The results revealed that impaired diffusion was more common than reduction of vital capacity. Detailed studies, including measurement of the minute ventilation and calculation of the vital capacity, timed vital capacity, and maximal midexpiratory flow rate from a spirometric tracing, measurement of the diffusing capacity of the lung by the steady-state carbon monoxide technique, determination of arterial blood gas composition, and cardiac catheterization for measurement of right heart pressures and cardiac output, were performed on 12 of the 47 patients. The results of these studies revealed consistent reduction of the diffusing capacity despite variable reduction of vital capacity and normal or elevated pulmonary arterial pressure. Reduction of the diffusing capacity of the lung is the most consistent functional abnormality observed in patients with pulmonary fibrosis.

VII. Comparison of Isoniazid Alone with Isoniazid-PAS in the Original Chemotherapy of Noncavitary Pulmonary Tuberculosis: Results from the Veterans Administration-Armed Forces Co-operative Study on the Chemotherapy of Tuberculosis. S. Philips. Am. Rev. Resp. Dis. 80:641-647 (Nov.) 1959 [New York].

The author reports on 282 patients with pulmonary tuberculosis, who were treated on the pulmonary disease service of the Veterans Administration Hospital in Memphis, Tenn., 134 of them being treated with isoniazid alone, while 148 were treated with isoniazid and aminosalicylic acid (PAS). One hundred eighty-nine of the 282 patients were treated for 5 to 8 months, and of these, 94 received isoniazid alone and 95 were given isoniazid and aminosalicylic acid. The proportion of minimal and moderately advanced cases, the incidence of progressive disease, and the occurrence of bilateral lesions were almost identical in the 2 groups of patients. Other factors, such as race, sex, and thoracic surgical treatment preceding the chemotherapy, were also similar. However, the group of patients treated with isoniazid and aminosalicylic acid contained more young patients and less patients of advanced age than did the group treated with isoniazid alone.

The therapeutic results obtained with isoniazid alone in patients with minimal or noncavitary moderately advanced disease appeared to be probably equally as good as those obtained with isoniazid and aminosalicylic acid. The reversal of infectiousness, roentgenographic improvement, achievement of "target point" (i. e., that point in treatment at which the sputum becomes free of tubercle bacilli, and roentgenographic abnormalities have become stable, and all tuberculous cavities have closed), and the incidence of isoniazid resistance were practically identical in all the patients treated with isoniazid alone for periods up to 8 months and in those who also received aminosalicylic acid. In addition, with isoniazid alone there was an obvious saving in cost and less drug toxicity than when isoniazid was given in combination with aminosalicylic acid.

Pasteurella Multocida Infections in Man: Report of 2 Cases—Meningitis and Infected Cat Bite. M. N. Swartz and L. J. Kunz. New England J. Med. 261:889-893 (Oct. 29) 1959 [Boston].

Pasteurella multocida is a small, nonmotile, gram-negative, ovoid rod showing bipolar staining. Although it is primarily a pathogen in the animal world, occasionally infection due to Past. multocida occurs in man, and cases have been described with increasing frequency since the early reports of Brugnatelli in 1913 and of Hundeshagen during the 1918 influenza pandemic. The majority of human infections caused by Past. multocida follow one of 3 clinical patterns. The most common comprises cases of local infection with adenitis after cat bites. These progress commonly to osteomyelitis of the underlying bone. The second pattern is one of chronic pulmonary infection in which this organism may occur as the primary pathogen or in association with other organisms. Cases of bronchiectasis, and rarely of empyema, have been reported; the organism has been cultured from infected nasal sinuses as well. In the third pattern, a systemic form of infection with meningitis or bacteremia has occurred. Although wound infection with Past. multocida is commonly associated with a history of exposure to animals, only about half of the patients with meningitis or systemic infection with the organism present such a history.

The first of the 2 cases of Past. multocida infections presented concerned a 62-year-old woman who sustained a cat bite on the wrist and hand. It was a typical example of the commonest form of human infection with Past. multocida. First, cellulitis developed, and 5 weeks after the cat bite, x-ray study of the wrist showed a small area of osteolysis in the distal radius, strongly suggestive of osteomyelitis. Recovery was complete on a program of local heat and penicillin. The second patient was an 83-year-old man in whom the onset of meningitis was sudden. Because of the variability of the organisms on smear, some suggesting meningococci and others small gram-negative rods, the patient was treated with chloramphenicol and penicillin. The patient's condition deteriorated, and seizures occurred; streptomycin was administered intrathecally and parenterally. The patient died 72 hours after admission to hospital. By this time the organism had been identified as Past. multocida, and the identification was verified.

While there is a large animal reservoir of Past. multocida, cats and perhaps dogs are the commonest sources of contact for man. The pleomorphism of this organism on smear has led, on several occasions, to mistaken diagnoses of Neisseria intracellularis, Hemophilus influenzae, and Mima polymorpha infection. Precise immunological methods are now readily at hand for definitive identification of this organism. Specific etiological diagnosis of this agent in systemic infections is most important, since penicillin appears to be the antibiotic of choice, and would not ordinarily be considered in the treatment of infection due to a gram-negative bacillus.

Sequential Use of Paired Combinations of Isoniazid, Streptomycin, Para-Aminosalicylic Acid, and Pyrazinamide: A United States Public Health Service Tuberculosis Therapy Trial. H. Curtis, F. W. Mount, S. H. Ferebee and others. Am. Rev. Resp. Dis. 80:627-640 (Nov.) 1959 [New York].

A United States Public Health Service tuberculosis therapy trial was performed on 1,882 patients, over 15 years of age, in 25 hospitals. The patients were given 2 16-week courses of antituberculous drug therapy with isoniazid, pyrazinamide. aminosalicylic acid, and streptomycin in paired combinations which were tested against a 32-week course of isoniazid and aminosalicylic acid. The daily dose of isoniazid ranged from 4 to 6 mg. per kilogram of body weight. The daily dose of pyrazinamide ranged from 35 to 45 mg. of body weight. Aminosalicylic acid was given in a daily dose of 10 to 12 Gm. Streptomycin was given in doses of 1 Gm. daily or twice a week. Clinical, bacteriological, and roentgenographic examinations were made at 4-week intervals throughout the trial. All cultures of tubercle bacilli obtained were tested in one laboratory for susceptibility to all 4 drugs.

Three regimens—(1) isoniazid with aminosalicylic acid, switching to streptomycin twice weekly with pyrazinamide, (2) isoniazid with pyrazinamide, switching to streptomycin twice weekly with aminosalicylic acid, and (3) streptomycin twice weekly with pyrazinamide, switching to isoniazid with aminosalicylic acid—showed no therapeutic superiority over a 32-week course of isoniazid with aminosalicylic acid and produced twice as many toxic reactions. The 4th regimen tested, namely, daily administration of streptomycin with pyrazinamide, switching to isoniazid with aminosalicylic acid, was therapeutically superior to continuous administration of isoniazid with aminosalicylic acid, although 3 times as many patients were unable to tolerate one or more of the drugs used. For patients with far-advanced cavitary disease, this regimen's higher rate of drug intolerance was outweighed by its therapeutic advantage. It would appear that only 12 weeks of daily administration of streptomycin with pyrazinamide, followed by 20 weeks of administration of isoniazid with aminosalicylic acid, would be less toxic and therapeutically even more effective for these patients.

Value of Lugol Test in the Differential Diagnosis of Hemorrhages of the Upper Digestive Tract. H. W. Pinotti and A. Raia. Rev. Assoc. méd. brasil. 5:249-256 (Aug.) 1959 (In Portuguese) [São Paulo, Brazil].

A serum precipitating Lugol test was given to 50 patients with hemorrhage of the upper digestive tract, treated at the Hospital das Clínicas, University of São Paulo, Brazil. There were 41 males and 9 females, between the ages of 14 and 71 years. The reagent used was Lugol's solution, containing 20 Gm. of metallic iodine and 40 Gm. of potassium iodide in 300 cc. of distilled water. The test was made with 2 or 3 cc. of blood taken from a vein before any transfusion had been given to the patient. The Lugol test is positive when the mixture of a drop of the solution and a drop of serum causes a precipitate. In the negative test the mixture remains transparent, with no serum precipitation. Additional tests given the patients in this study were determination of blood proteins, blood count, roentgenologic examination, and esophagogastric endoscopy. The Lugol test was positive in 24 patients; 19 of these patients had hepatic cirrhosis, 3 had a liver disease associated with gastroduodenal ulcer, and 2 had an advanced gastric cancer. Of the 26 patients with negative results, 23 had peptic ulcer (duodenal in 16, gastric in 5, and gastroduodenal in 2), 1 had gastritis, and 2 had gastric cancer. In the series as a whole, the test was positive in all the patients with portal hypertension and negative in all those with gastroduodenal ulceration. The diagnosis established by the test was confirmed surgically and histologically. The results of the Lugol test were instrumental in orienting the treatment given to all 26 patients with a negative reaction, and to 21 (87.5%) of the 24 with a positive reaction.

The authors conclude that the Lugol test, giving a positive reaction in patients with hepatic cirrhosis and a negative reaction in patients with gastroduodenal ulcer, is fairly effective in establishing the differential diagnosis in hemorrhage of the upper digestive tract. The positivity or negativity of the test is a result of the level of blood proteins. The patients with cancerized gastric ulcer give a positive Lugol reaction even when there is no evident hepatic lesion; in such cases the test loses its diagnostic value. The Lugol test should be performed during the hemorrhagic crisis and with blood taken before any therapeutic transfusion is given.

Cardiopulmonary Function in Chronic Obstructive Emphysema. M. H. Williams Jr. and L. R. Zohman. Am. Rev. Resp. Dis. 80:689-699 (Nov.) 1959 [New York].

The authors performed ventilatory studies and measurements of pulmonary vascular pressures and flows, of diffusion of gases in the lungs, and of arterial blood gas composition during rest and exercise on 22 men with chronic pulmonary emphysema, who were moderate-to-heavy cigarette smokers of long standing. The results of these studies revealed severe and persistent reduction of the maximal midexpiratory flow rate and vital capacity; consistent reduction of the carbon monoxide diffusing capacity, as measured by the steady-state technique during both rest and exercise; mild hypoxemia and carbon dioxide retention at rest, slightly increased by exercise; increased residual volume of the lungs, with impaired mixing of gases in the lungs; increased lung dead space; pulmonary hypertensions, which was mild at rest but fairly severe during exercise; and a cardiac index, which was normal at rest but subnormal during exercise.

From these results the pathophysiology of chronic pulmonary emphysema emerges as a relatively homogeneous picture of persistent severe airway obstruction and reduced diffusing capacity. The latter was interpreted as a reflection of the reduced alveolar-capillary surface area, which is the pathological criterion of emphysema. By calculating the effects of the reduced alveolar ventilation, low diffusing capacity, and measured right-to-left shunt in these patients, it was found that the major contribution to hypoxemia was the presence of disordered relationships between ventilation and perfusion in the lung.

SURGERY

Therapy of Bronchial Carcinoma. H. Kunz. Wien. klin. Wchnschr. 71:720-723 (Sept. 25) 1959 (In German) [Vienna].

The author reports on 759 patients with bronchial carcinoma, who were admitted to the second surgical clinic of the University in Vienna during the last 3 years. Radical surgical treatment by pulmonary resection of the involved lung or lobe was performed in only 254 patients (33.5%). One of the reasons for the appallingly large number of patients with inoperable disease is the fact that the initial symptoms of bronchial carcinoma, when the disease is still in a stage offering relatively good chance of cure, frequently are highly insignificant. Not only the patient but, unfortunately, also the physician often does not pay enough attention to an increased smoker's cough, with little expectoration and occasional minute amounts of blood in the sputum of a person who looks well, but whose chest roentgenogram, when taken, may already reveal an extensive bronchial tumor. One more reason may be found in diagnostic difficulties, since a peripheral carcinoma particularly may be completely symptomless for a prolonged period and may be interpreted as a benign process or an inactive tuberculoma on routine roentgenologic examination. Of 56 patients with round shadows who were operated on, 34 (60%) proved to have a peripheral bronchial carcinoma.

Definitive signs of inoperability are supraclavicular or axillary lymph node metastases, paresis of the diaphragm on the side of the bronchial carcinoma, invasion of the thoracic wall with destruction of ribs, and the finding that the tumor has advanced from the main bronchus into the trachea. There is a high probability that the tumor is inoperable when the tomogram shows enlarged hilar lymph nodes or lymph nodes adjacent to the mediastinum, when the carina has a flat instead of a pointed appearance on endoscopic examination, and when a hemorrhagic exudate and pain in the area of the thoracic wall are present. Most of the patients with bronchial carcinoma are of advanced age, and, therefore, operability also depends on their adaptability to the reduced breathing surface and on their powers of resistance not only during the immediate postoperative period but also in the future. Pulmonary function tests, with determination of residual volume, maximum breathing capacity, and volume of air expired within one second, are of great aid in deciding whether a pneumonectomy or a lobectomy is advisable in the individual patient.

Although the mortality rate among patients in the 7th decade of life is much higher than among those of less-advanced age, the author believes that pneumonectomy can be justified in some patients over 70 years of age, in whom the preoperative examinations gave favorable results, but, as a rule, lobectomy should be performed in this age group. Twenty-eight per cent of the patients, who were in the 7th decade of life when undergoing pneumonectomy, were alive 3 years after the operation, in contrast to none of those who were considered to have inoperable disease or who did not submit to surgical treatment. Permanent cures were obtained in 20 or 25% of the patients operated on, and the operative mortality rate was 17.7%, including patients who had been considered poor surgical risks and all those in whom the disease was far advanced. Of patients operated on during the 6th decade of life, 38% were still alive 3 years after the operation, and of patients undergoing lobectomy in the absence of lymph node involvement, 40% were still alive after 3 years. The 3-year survival was chosen, because it was found that most of the patients operated on, who died, did so within the first 3 years.

Energetic symptomatic therapy after occasional roentgen irradiation and chemotherapy is of greatest importance in patients with inoperable disease. Sulfonamide preparations and antibiotics should be given to patients with inflammatory pulmonary complications resulting from bronchial stenosis; cough due to irritation should be combated with codeine and dihydrocodeinone bitartrate (Dicodid). Administration of alkoloids should not be instituted too early, but neither too late. Temporary relief of pain may be obtained by infiltration of the intercostal nerves with procaine hydrochloride. Courses of injections of a proprietary compound extract of testis, cerebral lipids, and amniotic fluid proved to have a favorable effect on the general condition of the patient, and administration of small doses of cortisone frequently improved the subjective condition.

Results Following Conservative Treatment of Fractures of Tibial Shaft. W. D. Holderman. Am. J. Surg. 98:593-597 (Oct.) 1959 [New York].

The author analyzes the results obtained in 55 patients who were treated for fracture of the tibial shaft at the University of Kansas Medical Center in Kansas City from 1950 to 1957. For the most part the patients included in this series were severely injured or had unstable fractures. Of the 9 children, 8 had closed fractures and 1 had an open fracture. Of the 46 adults, 17 had open fractures and 29 had closed fractures. Six of the 9 children and 38 of the 46 adults had associated fractures of the tibia. Skeletal traction was used in the initial stage of treatment in 58% of the patients. A Steinmann pin was drilled through the os calcis for application of the traction, and the extremities were all supported on Böhler frames. None of the tracts made by the pins became infected. A brace was used at some stage of ambulation in 30 of the adults and in 1 of the children. The usual brace was a tibial tuberosity weight-bearing brace with 2 side-irons rigidly attached to the shoe and a leather lacer fracture cuff. Exceptionally, an ankle joint was included, usually for fractures in the distal extremity of the tibial shaft. The use of the brace contributed to the patient's comfort and early rehabilitation.

The one child with an open fracture had been subjected to débridement and closure elsewhere. At the Kansas Medical Center angulation was corrected by means of manipulation and application of a long-leg plaster cast. A long-leg plaster was used in all the children, but in 2 its application was preceded by initial skeletal traction. Closed methods have been safe and reliable in this small group of children with fractures of the tibial shaft.

Of the 29 adults with closed fractures, 7 were treated by manipulation and a long-leg plaster, 21 by skeletal traction, and 1 by open reduction, fixation with screws, and long-leg plaster. Vascular impairment leading to gangrene and requiring disarticulation of the knee occurred in one, and peroneal nerve palsy occurred in another of these 29 patients. Closed treatment of closed fractures of the tibial shaft in adults has been safe, economical, and reliable.

The results obtained in the 17 open fractures of the tibial shaft in adults have been far less satisfactory. The severity of the initial injury, as indicated by the necessity for closure with a pedicle graft, and infection of the primary wound have been associated with a high incidence of nonunion and amputation. Further breakdown of the infections indicates that in all the patients with primary mild infections the fractures eventually healed (one with delayed union). A primary severe infection in one patient resulted in amputation; one patient (without union of the fracture) committed suicide; and in one the fracture healed. In 2 of the patients with infection after bone graft, amputation was necessary; in the third, the fracture healed, but there is still slight drainage. Analysis of the 5 cases of delayed union and nonunion discloses that 2 of these patients were treated by skeletal traction, 2 in long-leg plasters, and 1 with initial fixation with plate and screws. The fractures eventually healed in 13 of the 16 surviving adults with open fractures.

Experience in Current Surgical Treatment of Bronchiogenic Carcinoma. E. de Jesús Zerbini, A. Jatene, G. Verginelli and others. Rev. paulista med. 55:91-100 (Aug.) 1959 (In Portuguese) [São Paulo, Brazil].

Two hundred sixty-two patients with bronchiogenic carcinoma were observed in the department of surgery of the Faculty of Medicine, University of São Paulo, between 1946 and 1957. Seventy-eight patients (29.7%) had clinical symptoms which contraindicated surgical treatment; 87 were found to have an irresectable tumor at thoracotomy; and 97 underwent pulmonary resection. Seventy-four pneumectomies, 20 lobectomies, and 2 segmental resections were performed. The most frequent causes of contraindication for resection were neoplastic invasion of supraclavicular or axillary lymph nodes, ascertained by biopsy; mediastinal metastases; hemorrhagic pleural effusion; distant metastases; diaphragmatic or vocal cord paralysis; and cardiopulmonary insufficiency. Pulmonary resection was possible in 37.9% of the patients whose symptoms had started 6 months or less before the hospitalization, in 36% of those with symptoms of 7 to 12 months' duration, and in 34.2% of those with symptoms for more than one year. The rate of irresectability was 85% for the 47 tumors in the main bronchial tree, 55.3% for the lobar or segmental tumors, and 41.5% for the 65 peripheral tumors. The most frequent histological type of carcinoma was the undifferentiated one, found in 101 patients. There were 83 squamous-cell tumors, 36 adenocarcinomas, 3 alveolar carcinomas, and 39 unidentified tumors.

Eighty-one of the 97 patients who underwent pulmonary resection survived for periods which varied from 6 months to 5 years. Although there was a correlation between the operability of the tumor and the duration of the symptoms, the localization, and the histological type, there was no correlation between these factors and survival. Of the 7 patients who had survived 5 years at the time of the follow-up, 2 had had squamous-cell carcinoma of the bronchial tree, 2 had had a lobar tumor (1 adenocarcinoma and 1 undifferentiated), and 3 had had a peripheral tumor (2 undifferentiated and 1 squamous-cell).

Adrenal Autotransplantation in Cushing's Syndrome. C. Franksson, G. Birke and L.-O. Plantin. Acta chir. scandinav. 117:409-415 (no. 5) 1959 (In English) [Stockholm].

The authors resorted to autotransplantation of adrenal tissue in 5 women with adrenal cortical hyperfunction (Cushing's syndrome) arising from adrenal cortical hyperplasia. The aim of surgery in Cushing's syndrome is to diminish the adrenal steroids and thus cause the pathological manifestations to disappear. Total adrenalectomy guarantees this result. It also renders the patient totally dependent on exogenous steroids. By making the adrenalectomy subtotal, one tries to avoid this drawback. Then, however, one runs the risk of removing too little tissue and thus necessitating another operation. Adrenal autotransplantation produces the advantages of subtotal adrenalectomy (no, or low, requirements of exogenous steroids) without its main disadvantage (risk of another major operation).

The patient was placed in the prone position, and both adrenals were explored simultaneously through subcostal, extrapleural, extraperitoneal incisions. When diffuse hyperplasia of both adrenals was present, the adrenals were excised and placed in a sterile metal container which stood in crushed ice. It was hoped that the low temperature would slow down the autolytic processes in the transplants. The patient was then turned to the supine position, and adrenal tissue was implanted in the sartorius muscle. The amount of tissue transplanted varied. No steroids were given preoperatively. When the second adrenal had been removed, an intravenous drip infusion of hydrocortisone (100 mg. of hydrocortisone in 1,000 ml. of 5.5% dextrose solution) was begun. Twelve hours later this was replaced by intramuscular injection of cortisone (50 mg. 4 times in 24 hours). The dose was gradually reduced in the following week to 25 mg. by mouth twice daily. A maintenance dose of varying size (25 to 50 mg. daily) was subsequently given. When the adrenal transplants were assumed to have begun to function, substitution therapy was discontinued. No important complications occurred in association with surgery. In all 5 women Cushing's syndrome disappeared more or less completely.

Endometriosis of the Large Intestine. R. E. B. Tagart. Brit. J. Surg. 47:27-34 (July) 1959 [Bristol, England].

Endometriosis of the large intestine is rare, very much rarer than carcinoma. Seventeen out of the 21 cases, on which this report is based, were found in the records of a hospital (over a period of 17 years), in which carcinomas of the rectum are found at the rate of about 150 per year. The remaining 4 cases were from another hospital. It is possible that endometriosis of the large intestine develops in from 1 to 2% of women during their menstrual life, but the great majority of these lesions cause no symptoms. Direct transperitoneal implantation and cellular metaplasia are probably the most important etiological factors. The size of the lesions varies from pinhead nodules to tumors, 5 cm. in diameter. The lesion is usually situated in the subserous or muscular coat of the intestine The main bulk of the tumor is made up of fibrous tissue, contraction of which may cause intestinal obstruction. When the lesion penetrates to the mucous or submucous layer, its histological appearance comes to resemble that of carcinoma. The tumor is hormone dependent.

In 5 of the 21 cases the endometrioma was an incidental lesion, the major disease being carcinoma. These cases have been excluded from the sections dealing with clinical features, treatment, and prognosis. Three perineal lesions are included. These 3 patients complained of a tender lump near the anus; one of these patients had 2 lumps under the perineal skin. Reviewing the clinical aspects of the women with abdominal lesions, the author shows that the patients fall into 2 groups: those with obstructive and those with irritative features —colic and diarrhea. Seven out of 11 patients said that their symptoms were more severe just before or during a menstrual period, but the absence of these does not exclude the diagnosis. Physical examination revealed no abnormality in 5 patients; in 3 there was evidence of subacute intestinal obstruction; in 3 a hard mass presumed to be a carcinoma was felt in the rectum, while in 1 a tender swelling, lying behind the uterus, was felt through the rectal wall. Representative case histories are presented. One of these patients had purely obstructive symptoms; in another one the symptoms were those of intestinal irritation; and in a third one there was a combination of irritative and obstructive features, the latter replacing the former as fibrosis as the endometrioma progressed.

Preoperative diagnosis is rare, but it is important to interpret correctly the findings at operation. This was done in 5 out of 11 cases. In 5 others the lesion was thought to be a carcinoma, and in 1 case no diagnosis was made. The growth appears either as a hard tumor or as a string-like stricture in the wall of the intestine. It is almost indistinguishable from a carcinoma. A correct diagnosis depends on the recognition of associated pelvic endometriosis. Where the characteristic small red plaques of endometriosis are visible in the subserous coat of the intestine, adjacent to the tumor, there is little difficulty, but when the lesions are more distant, such as ovarian "chocolate cysts" or scattered peritoneal endometriomas, the relationship is less obvious. Moreover, intestinal carcinoma may be associated with pelvic endometriosis. Diagnosis by barium enema depends on recognition of the absence of mucosal ulceration at the site of the lesion. Sigmoidoscopic findings are difficult to distinguish from carcinoma, and biopsy specimens may also resemble those of carcinoma. A correct preoperative diagnosis was made in 1 out of 16 cases. Five of 11 abdominal cases were diagnosed at operation. If possible, the lesion should be excised, intestinal continuity restored, and one or both ovaries preserved. If excision of the endometrioma can only be achieved at the price of a permanent colostomy, bilateral oophorectomy is likely to cure the disease and is a preferable treatment. When pelvic fibrosis is very extensive, a permanent colostomy may be necessary.

Resection of the Pre-aortic Plexus by the Method of Arnulf: Palliative Treatment of Angina Pectoris. I. Grewald. Acta chir. scandinav. 117:351-355 (no. 5) 1959 (In English) [Stockholm].

Grewald points out that Arnulf first described his method of treating angina pectoris in 1939. It consists in the resection of the nerves which constitute the preaortic plexus, and which supply the coronary vessels with sensory, sympathetic, and vasoconstrictive fibers. The operation is performed under local anaesthesia, and even patients in a poor general condition stand it surprisingly well. A total of 52 patients (25 men and 27 women) with severe angina pectoris have been subjected to this operation in the Kommunehospital in Horsens, Denmark, and the observation periods are now long enough that it is possible to gain an impression of the value of this method of treatment. Patients were selected for operation only after medical treatment had failed. All had previously been treated in medical departments. The intensity and frequency of anginoid pain, the degree of disability, the dosage level of medication (in particular, of morphine), and positive findings in the cardiologic examinations were the criteria in the selection of the patients. Prior to operation, all the patients were subjected to roentgenographic and electrocardiographic studies. The ages of the patients ranged from 34 to 75 years. Seven patients had had angina pectoris for more than 10 years, 34 for from 1 to 10 years, and 11 for less than 12 months. Fourteen of the patients had previously had coronary thrombosis; 6 were, or had previously been, decompensated; and more than one-third of them constantly received morphine.

In 2 of the 14 patients who had died before this analysis was made (May 1, 1957), death was caused by the operation (4%). The 6 patients who died later as the result of their heart disease survived from 6 weeks to 3½ years after the resection of the preaortic plexus. Four patients died of other causes, and in the remaining 2 patients the cause of death was not known. Two of the 38 surviving patients could not be traced. Only 3 of the other 36 patients were completely free from angina pectoris, while the operation had resulted in considerable improvement in 8, i. e., good results were obtained in 30% of the cases. In another 13 patients (36%) some improvement had occurred, while the operation had given no relief in the remaining 12 patients (33%). The average length of the observation periods in the 11 patients with good results was 49.3 months. The results of the analysis suggest that poor results are obtained when angina pectoris is complicated by severe neurosis.

Staphylococcal Endocarditis Following Mitral Valvotomy: With Special Reference to Coagulase-Negative Staphylococcus Albus. L. Resnekov. Lancet. 2:597-600 (Oct. 17) 1959 [London].

Of 70 consecutive patients treated by mitral valvotomy, 10 developed staphylococcic endocarditis. Petechia and mycotic aneurysms were not seen, and retinal lesions only once. Enlargement of the spleen was noted in 2 patients. A raised sedimentation rate, anemia, and clubbing were the clearest guides to the cause of pyrexia. A change of heart murmur, not explainable by the operation itself—e. g., the development of the murmur of aortic incompetence—was also significant. In some patients infection was apparent almost immediately, in others in 2 to 4 weeks, and in still others after a longer period of time. The infective organisms were coagulase-negative staphylococci alone in 5 patients and coagulase-positive alone in 1. In the other 4 patients, blood cultures yielded Staphylococcus aureus at first but later only the coagulase-negative staphylococci. Erythromycin seems to have given the best results. It was used either alone or in combination in 8 of the 10 patients. Often treatment was started with another antibiotic, but only when this was changed to erythromycin did the temperature come down.

Three patients have died; in 2 death was due to infection uncontrolled by antibiotics individually or in combination. In the third patient, congestive heart failure due to valvular damage resulting from the infection was the immediate cause of death. One patient had recurrence of the infection. Of the remaining 6 patients, it is still too early to draw conclusions. One of these patients has remained well for many months. The actual source of the infection is often difficult to determine, but special attention must be paid to precautions in the operating theater.

Subphrenic Abscess: A Clinical Study of 101 Cases. J. Wetterfors. Acta chir. scandinav. 117:388-408 (no. 5) 1959 (In English) [Stockholm].

The author reviews observations on 101 patients with subphrenic abscess, who were treated in 2 hospitals in Sweden from 1940 to 1956. There has been a shift of the peak incidence toward higher ages, probably because of the increased number of elderly people in the population. Peptic ulcer and biliary tract diseases are nowadays the most important factors in the etiology of subphrenic abscesses, and this is explained by the increase in these diseases during the past decades and the wider use of surgical treatment. In more than half of the cases the abscesses followed abdominal operations. Three different routes of spread of the infection to the subphrenic region are maintained according to the literature—the intraperitoneal, the lymphatic, and the hematogenous. In the cases in which the author was able to investigate the mode of spread, he found that the infection from neighboring foci (ulcers, infected gallbladders) always spread by the intraperitoneal route. A purulent streak, or remnants of one, extended from the focus of origin (in most instances, via a subhepatic abscess or accumulation of exudate) to the subdiaphragmatic space, around either the anterior or the lateral margin of the liver. Lymphatic spread was not verified in any of the cases. In most of the cases of spread from distant foci, the abscess was produced by direct intraperitoneal spread, or was a residual one following general peritonitis.

The author, in contrast to many other observers, did not find that the mortality was influenced by the time elapsing between the development of the abscess and its drainage. Symptoms and signs only suggest the possible presence of a subphrenic abscess; the diagnosis rests mostly on roentgenologic evidence. The slightest deviation from a normal course after laparotomy or in case of intra-abdominal infection is an indication for roentgenologic examination. The cardial signs are pleural exudate, abolition of the movements of the diaphragm, elevation of the diaphragm, the presence of gas, and displacement of viscera.

Both surgical and conservative treatments were used in this series of patients. Conservative treatment with repeated roentgenologic control proved to be effective. The drugs employed were penicillin, streptomycin, Chloromycetin, Aureomycin, and Terramycin. The mortality was low with conservative treatment. If regression, with absorption of the abscess, does not seem to occur, surgical drainage should be instituted. This can be performed in a stage of lowest possible virulence, the drainage being made by the extraserous approach. With this method the risk of fatal intrathoracic and intraabdominal complications is smallest, and the prognosis most favorable.

Radiologic Changes in 15 Patients with Interauricular Communication Operated on under Extracorporeal Circulation. J. H. Medeiros Sobrinho, J. S. Perfeito, S. Paladino and others. Rev. paulista med. 55:191-203 (Sept.) 1959 (In Portuguese) [São Paulo, Brazil].

Fifteen patients (10 females and 5 males), whose ages ranged from 6 to 32 years, were treated surgically for an abnormality of the interauricular septum. In 3 of them there was also an abnormal return of the pulmonary venous blood which flowed into the right auricle. All the patients were catheterized preoperatively, and 3 were recatheterized a year after the operation. The study of the roentgenologic changes was made from 1 to 12 months after surgery. The changes were evaluated by comparing the size of the defects, as measured during the operation, and the preoperative pressure in the right heart chambers and in the pulmonary artery with the postoperative findings.

The patients were classified into 4 groups in relation to the results regarding the heart hypertrophy: 1. Two patients with a normal-sized heart and an abnormal morphology showed no roentgenologic changes. 2. Five patients with a slightly enlarged heart showed a moderate reduction of the hypertrophy after the operation. 3. Three patients with a moderately enlarged heart showed a great reduction in size. 4. Five patients with a considerably enlarged heart showed a considerable reduction in size. Regarding the pulmonary circulation, the lungs, which in the preoperative roentgenogram lacked transparency because of the congested vessels, were shown in the postoperative roentgenograms with a normal transparency as a result of the reduction of the congestion. The authors conclude that the roentgenologic improvement was not correlated with the mechanism of the changes observed, with the pressures in the right cardiac chambers, with the pressure in the pulmonary artery, or with the size of the abnormalities. Although the greatest degree of regression was observed in the patients with a very enlarged heart and a markedly abnormal vascular roentgenologic image, the highest degree of normalization was achieved in those with a moderate degree of cardiac hypertrophy and pulmonary congestion.

The Problem of Spontaneous Rupture of the Normal Alimentary Canal. K. Cronin. Brit. J. Surg. 47:43-50 (July) 1959 [Bristol, England].

The term "spontaneous" when applied to rupture of the alimentary tract is sometimes regarded as synonymous with "idiopathic," but a study of the new cases described in this paper and a review of literature reports suggest that in most cases an explanation can be given for a perforation of an apparently normal viscus. In 2 of the 6 patients whose histories are presented, the perforation involved the esophagus. The first of these 2 patients was a 77-year-old man who, while drinking beer, suddenly felt nauseated. As soon as he started to vomit, he felt a sudden severe pain in his epigastrium, which quickly increased in severity, spreading all over his abdomen and radiating behind the sternum into his left chest. On examination, his abdomen was rigid, but moved slightly on respiration. There was surgical emphysema at the root of the neck on both sides. On the basis of a clinical diagnosis of spontaneous rupture of the esophagus, thoracotomy was performed 7 hours after the onset of symptoms. A linear tear was found in the normal anterior wall of the esophagus. The rent was repaired, and the patient recovered.

The second patient with esophageal perforation was a 14-year-old boy who had sustained a severe gunshot wound of the right side of his head. There was an open wound in the right temporal and zygomatic regions, through which a cerebral fungus, 3 cm. in diameter, was protruding. The patient died 5 hours after bifrontal bur holes were made, and postmortem examination revealed, among other lesions, a hole in the esophagus. In connection with this case, the author mentions the curious relationship between gastric or duodenal ulceration and intracranial lesions, but he also says that, in analyzing postmortem reports of 300 patients admitted to a neurosurgical unit, he found only 2 with ruptured esophagus. Esophageal ruptures are always longitudinal and generally within the lower third of the organ.

Of the remaining 4 spontaneous ruptures, 1 involved the stomach, 1 the small intestine, and 2 the colon. The perforation of the stomach occurred in a 61-year-old man. Of the intestinal perforations, 1 occurred in an infant and 2 in adults.

The causes of spontaneous perforations include a sudden rise in the intraluminal pressure in a hollow viscus, closed at both ends. It is under such conditions that the esophagus and stomach rupture. Intestinal perforation may occur when the intraluminal pressure suddenly increases in one segment of the intestine without a corresponding rise outside this segment. Such a set of circumstances occurs in a patient with an inguinal hernia, who suddenly contracts the abdominal muscles. The mechanism is discussed. Defects in the muscular coat of the intestine—congenital, in infants, and acquired, as in adults with diverticulosis—may so weaken the intestine that it ruptures under minimal strain. Infective ulceration of the intestine is probably the cause of many of the perforations found in neonates. There is a small group of cases of spontaneous rupture of the intestine in adults, for which so far there is no satisfactory explanation.

Atelectasis of Lower Left Lobe as Complication After Certain Heart Operations. H. O. Ahnlung, L. Björk and H. Lodin. Thoraxchirurgie 7:348-353 (Oct.) 1959 (In German) [Stuttgart, Germany].

In postoperative roentgenologic control examinations after certain operations on the heart, the authors frequently observed atelectasis of the lower left lobe of the lung. As a rule, the atelectasis involved the entire lobe, but in some cases only the apical segment of the lower lobe was atelectatic. There was no air in the parenchyma, whereas the larger bronchi were air-filled. Thus, this is not an obstructive atelectasis, such as may result from stagnation of the secretions. The authors made studies on 184 patients who were operated on between 1955 and 1958. A tabulation of the patients reveals that the lower lobe atelectasis occurred in about half of the patients operated on for patent ductus arteriosus or for coarctation of the aorta, in about two-thirds of those operated on for pulmonary stenosis, and in nearly all of those operated on for atrial septal defect or for mitral stenosis.

The atelectasis does not occur immediately after the operation, but rather after a day or two, or later, but never later than the 7th postoperative day. It usually persists unchanged for 5 or 6 days and then gradually disappears in the course of several days. In some cases it persisted up to 3 weeks and than subsided slowly, in a few cases remnants being still visible 3 months later. In the majority of cases the lower lobe atelectasis was the only pulmonary complication, but in 4 cases the entire left lung was atelectatic; extensive pleural effusion occurred on the left side in 5 cases, atelectasis of the right side in 2 cases, and pneumothorax, of either the right or the left side, in 4 cases. The lower lobe atelectasis caused practically no symptoms. The authors suggest that mechanical factors are chiefly responsible. They are of the opinion that pericardiotomy, with subsequent effusion into the pericardium, is the chief cause and recommend that suture should be avoided and the pericardium should be left open. Intensive respiratory gymnastics were carried out before, as well as after, the operation. While this did not prevent the development of the atelectasis, it did prevent serious symptoms.

Large Hair Ball in Stomach of Male 58 Years of Age. A. W. Overgard and D. A. Sallis. Wisconsin M. J. 58:599-601 (Oct.) 1959 [Madison].

The man whose history is presented was hospitalized with rigidity and tenderness in the upper abdomen. He admitted having had nausea, vomiting, and gas distress for about 3 or 4 days. There had been some colicky pain in the upper abdomen on the left over a period of 8 months. The preoperative diagnosis was intestinal obstruction of unknown cause. The postoperative diagnosis was trichobezoar of a large size, and the pathological report was: "Hair of human origin." The patient had a stormy postoperative course and remained in the hospital about 6 weeks. Gastric suction was used continuously for about 2 weeks. Dehiscence of the wound occurred, but the patient recovered and returned to his occupation as a laborer in a lumber yard.

The trichobezoar was caused by a mental aberration, which induced the patient to eat hair. He related that during the war years he spent his time on the west coast working in a war munitions plant. His wife remained in her own community. He suspected her or being unfaithful to him, and he received sexual satisfaction by eating human hair, the source of which he refused to reveal. The trichobezoar measured 19 cm. at the greatest length and 9 cm. at the largest width; it was shaped like the stomach. There was also a smaller trichobezoar which the patient passed about a week after removal of the trichobezoar from the stomach. This small hair ball may have caused obstruction and some of the difficulties the patient experienced after operation; the smaller trichobezoar measured 7 by 2 cm.

Wound Infections, Surgical Gloves and Hands of Operating Personnel. E. E. Shouldice and C. J. Martin. Canad. M. A. J. 81:636-640 (Oct. 15) 1959 [Toronto].

A study was made on 430 swabs of the hands and gloves of operating personnel at the Shouldice Clinic, Toronto, in order to find out the causes of wound infection in surgery. This bacteriological study was carried out on the hands of operating personnel who did not come in direct contact with coagulase-positive Staphylococcus aureus found in discharging wounds or on infected dressings. This was because only aseptic wounds for the repair of hernias and associated conditions had been considered, as no other type of surgery was performed in this institution. Operating personnel prepared their hands daily with only a 2-minute scrub period, and not for 10 minutes as is recommended elsewhere. No swab, collected before and after the operation, grew pathogenic coagulase-positive Staph. aureus, which showed that the hands of the operating personnel, their sweat in the gloves, or the method of scrubbing had not been a cause of wound infection.

The study revealed that punctured gloves were used in 61% of the operations performed in this series, whereas the over-all infection rate was 1.8%. Prophylactic antibiotic treatment was given to 4% of the patients, and those in whom wound infection occurred during this investigation did not receive prophylactic antibiotic treatment. In this study the incidence of infected wounds was actually greater in cases in which no glove perforations could be demonstrated than in those in which punctures were proved. In 1957 there were 3,303 herniorraphies performed in the Shouldice Clinic, with an infection rate of 1.2%. Prophylactic antibiotic treatment was given to 5% of the patients.

Functional Results Following Subtotal and Total Colectomy with a Re-establishment of Continuity. J. P. Glaubitz and J. W. McElwain. Surgery 46: 656-663 (Oct.) 1959 [St. Louis].

Subtotal and total colectomies with reestablishment of continuity have become accepted surgical procedures in the management of certain colonic conditions. This report describes observations on 11 patients (6 women and 5 men), of an average age of 50 years. Seven total colectomies and 4 subtotal colectomies were performed. Six of the total colectomies were for carcinoma, and the 7th was for ulcerative colitis. Two subtotal colectomies were performed for diverticulitis, one for adenomatosis, and one for a huge incisional hernia.

No deaths resulted in this series of 11 patients. Complications developed in 3 patients. In one patient a low-grade thrombophlebitis developed, which responded to administration of anticoagulants. A subdiaphragmatic abscess was evacuated in one patient, and a wound infection was drained in another patient. In some of the patients stool frequency increased at first, but 2 weeks after the operation stools became watery or soft, and at the end of 2 months they were formed and soft, with the exception of the patient with ulcerative colitis. In general, the patients subjected to subtotal colectomy had soft, formed stools somewhat earlier than patients undergoing total colectomy. By the third postoperative month, the evacuation habit appeared fairly well established, but in most cases additional improvement continued for 6 months. The 4 patients who had subtotal colectomy averaged 2 to 4 soft, formed stools daily, and the 7 patients who had total colectomy averaged 3 to 5. Although this stool frequency is somewhat higher than that reported by several other surgeons after colectomy, the authors feel that there was not enough intestinal malfunction subsequent to total and subtotal colectomy to warrant conservation if extensive resection appeared advisable.

Nasal Staphylococci and Sepsis in Hospital Patients. R. E. O. Williams, M. P. Jevons, R. A. Shooter, C. J. W. Hunter and others. Brit. M. J. 2:658-662 (Oct. 10) 1959 [London].

A preliminary analysis of studies on the incidence of cross-infection in one surgical ward at St. Bartholomew's Hospital in London had suggested that nasal carriers of Staphylococcus aureus suffered wound infection more often than noncarriers. The results described are derived from studies on 3 male surgical wards (A, B, and C) and 1 male medical ward (D). The analyses in the first half of the paper, on the nasal carrier state of 602 hospital patients, are based almost entirely on the records from ward A, while the analyses in the second half, relating nasal carriage to sepsis, are derived from the 1,358 patients in all 4 wards. Altogether, 38% of the 602 patients admitted to ward A carried Staph. aureus in their noses during the first week after admission to hospital; 13% of them carried staphylococci resistant to penicillin. There was a steady increase in the general carrier rate for staphylococci and in the rate of resistant strains in patients swabbed during their stay in hospital, so that, of the patients swabbed after 8 weeks in hospital, some 70% carried Staph. aureus in the nose, and half carried penicillin-resistant strains.

Patients who were noncarriers on admission acquired resistant strains in the ward more readily than those initially carrying sensitive strains. Of the patients who were noncarriers on admission, 30% had acquired resistant staphylococci by the third week in hospital, compared with only 18% of those who carried sensitive strains on admission. Of 165 patients treated with antibiotics, 64 acquired penicillin-resistant strains in their noses; 39 patients acquired tetracycline-resistant strains in their noses.

Of the 1,358 patients in the 4 wards, 722 underwent surgical operations. The incidence of staphylococcic wound sepsis was lower in patients who never yielded staphylococci from the nose during their stay in hospital than it was in patients who were found to be carriers. Staphylococcic wound sepsis developed in 7 (or 2%) of the 342 patients who were not nasal carriers at any examination, compared with 27 (7.1%) of the 380 patients who were carriers. Altogether, 18 of the 27 nasal carriers who developed postoperative sepsis yielded Staphylococcus organisms from their wounds of the type they harbored in their noses. The incidence of infection due to staphylococci different from those carried in the nose is presumably a measure of cross-infection direct to the wound, and one might expect that this would be independent of the nasal carrier state. In fact, 7 (2%) of 342 wounds in noncarriers developed sepsis, and 9 (2.4%) of 380 wounds in carriers developed sepsis due to staphylococci of a different type from those carried in the nose. Of patients who were nasal carriers of one or another of 10 apparently more virulent types, 35% had wound sepsis, in all cases due to the nasal type of staphylococci.

In 4.5% of 1,319 patients, sepsis developed elsewhere than in a wound. The relation to nasal carriage was very similar to that of wound sepsis. The results suggest that the incidence of sepsis might be reduced if acquisition of staphylococci in the nose could be prevented.

NEUROLOGY & PSYCHIATRY

Experimental Analysis of an Attempt to Improve Speech in Cases of Expressive Aphasia. S. Weinstein. Neurology 9:632-635 (Oct.) 1959 [Minneapolis].

The author points out that Birch and Lee recently described a dramatic improvement in the speech of 75% of expressive aphasics during and after binaural administration of a tone at 256 cps at an intensity of 60 db. In an effort to confirm the results of this simple procedure, the author tried it on 18 patients with expressive aphasia, who had minimal or no receptive difficulties. The symptoms ranged from mutism to moderate word-finding impairment. Some patients had additional slight dysarthria. The diagnosis was cerebral vascular accident to the left hemisphere in 16 cases and neoplasm in 2. All patients were right-handed prior to the onset of symptoms. They were tested from 1 to 32 months after the onset of symptoms. In each of 6 tests administered, the number of objects correctly identified or words or numbers correctly read was recorded, as well as the time required by the patients to respond correctly. The patient was allowed 30 seconds for each response. The tests included an object-identification test, a picture-identification test, a word-reading test, a color-naming test, a number-reading test, and a sentence-reading test.

After completion of the test under the silent condition, a tone of 250 cps at 60 db. was turned on for 30 seconds. At the end of this time, the test was repeated as before, with the binaural stimulation continuing throughout. If there was a question of hearing loss, audiometry was first conducted. In all cases in which hearing loss was demonstrated, the intensity of the tone was appropriately increased for each ear individually to insure that the patient was binaurally stimulated at 60 db. above threshold. Neither the group nor any individual patient demonstrated improvement on any test. Chance fluctuations in performance adequately describe the results of the stimulation. The author has no explanation to account for the failure of this study to confirm Birch's results.

An Approach to Psychiatric Consultation in the General Hospital. S. K. Schiff and M. L. Pilot. A. M. A. Arch. Gen. Psychiat. 1:349-357 (Oct.) 1959 [Chicago].

An approach to psychiatric consultation is presented, which the authors have found useful in the general hospital. It is primarily consultee-oriented rather than patient-oriented. A request for psychiatric consultation by a member of the house staff of a general hospital is a request for help. The reason expressed in the written consultation request may have little to do with what the consultant comes to see as the major problem. While the immediate focus of all consultation requests is the patient, in those instances in which the reasons seem unclear it may be useful to look at the consultee's implicit concerns, which he may be unable to deal with directly. The referring physician may find it difficult to express his major source of concern, particularly when he is in disagreement with colleagues or superiors. Four case histories are presented in each of which the stated reason for the consultation was not the referring physician's primary concern, which became evident only after careful scrutiny.

In the first case, the problem was one of highly personal conflict involving the intern and the resident responsible for the patient's care. The resident's dismay with the intern's performance and the intern's need to support a position of his own worth were crucial factors. In the second case, a request was made to stop a patient from leaving the hospital against medical advice. The effort to prevent this recalcitrant, provocative patient from leaving focused the house staff's misgivings over its responsibility for the patient's action. Although the question of how to "talk the patient into staying" precipitated the request for help, the house staff's questioning of its response to such a patient reflected a more basic concern. The feelings this patient provoked in the staff were discussed, and a rationale was offered for the patient's continued management in terms of both the patient's behavior and the staff's feelings.

The explicit concern of the consultee in the third case over the possible psychogenic origin of the patient's intractable abdominal pain served to introduce the entire area of the patient's treatment, management, diagnosis, and disposition for consideration. The house staff members had reached an impasse in management. The patient's demanding, depressed, and accusing behavior helped to provoke the house staff's annoyance and irritation. The fourth case illustrates the consequences of accepting the explicit reason for a consultation without adequately scrutinizing the implicit concerns. The consultant's reluctance to accept the house staff's lack of interest in what, to him, were interesting psychiatric problems and his need to use the consultation to demonstrate his skills and usefulness were the obstacles.

The manner in which the house staff sees the psychiatrist as a member of the hospital community, as well as the way in which the psychiatrist sees his own position, is extremely important in the consultation. The communication difficulties existing between the psychiatrist and the house staff are often responsible for the consultation going awry. Many of these difficulties are due to the consultee's inability to make his major concerns explicit to the consultant, whose first responsibility is to clarify what the major problems of the consultee are.

Is Lumbar Puncture Harmful in Multiple Sclerosis? K. Schapira. J. Neurol. Neurosurg. & Psychiat. 22:238 (Aug.) 1959 [London].

The origin of the belief that lumbar puncture is detrimental in patients with multiple sclerosis is difficult to trace, but some neurologists are quite emphatic about this procedure being contraindicated. Since this view is at variance with the author's experience, he decided to investigate this problem during a current survey of cases of multiple sclerosis in northeastern England, during which 700 patients were personally interviewed and examined. Inquiry was made as to whether lumbar puncture had been carried out at any stage of the illness, and also as to the course of the disease during the subsequent month. Of the patients questioned, rather less than half had been subjected to spinal puncture, and in 250 instances the information was considered sufficiently reliable for analysis. Of these, 231 patients reported their condition as unchanged, 14 patients reported improvement, and 5 patients considered that their condition had deteriorated. A second phase of the inquiry involved a comparison in 100 cases of the apparent course of the condition during the month after lumbar puncture with the tempo of progression evident during similar periods 12 months earlier and 12 months later. Here again it was found that lumbar puncture has little effect on the course of multiple sclerosis, and that any apparent effect occasionally observed is as likely to be favorable as deleterious. The risks of overlooking clinically atypical compression of the spinal cord are well known. There is clearly no reason to withhold the procedure in any case in which the faintest suspicion of such a lesion arises.

GYNECOLOGY & OBSTETRICS

Spontaneous Regression of Carcinoma of the Cervix: Report of a Case. P. E. Black and E. A. Brown. J. Maine M. A. 50:358-361 (Oct.) 1959 [Portland].

The authors report on a 73-year-old woman in whom, at the age of 61 years, diagnosis of squamous-cell carcinoma of the cervix was made at the Eastern Maine General Hospital, Bangor, 16 months after a vaginal hemorrhage. The diagnosis was confirmed by 2 separate biopsy and microscopic studies of the tissues. Standard treatment with 18 x-ray exposures, totaling 4,140 r, and 3,600 mg.-hr. of radium was without effect as judged by reexamination one year later. During the ensuing 2 years, however, there was a complete regression of the carcinoma. Subsequent roentgenograms and physical examinations, as well as 2 explorations of the abdomen during an appendectomy and a cholecystectomy, proved that neither primary nor secondary growths were present. The patient reacted anaphylactically to the use of iodopyracet (Diodrast). Although daily doses of 16 grains (1 Gm.) of morphine sulfate were originally required for intractable pain, when informed that the tumor was no longer present, the patient of her own volition refused further analgesics. She suffered no signs or symptoms of narcotic withdrawal, and needed neither substitute analgesic drugs nor treatment.

Eleven years have elapsed since the original diagnosis had been established, and 13 years have passed since the appearance of the first signs of any abnormality, and the patient is perfectly well and healthy. It is suggested that there may be a mechanism common to tumor regression, narcotic tolerance, and some allergic phenomena. Recent studies concerned with the immunological aspects of malignant disease point to this area of exploration.

Effect of Mothers' Smoking Habits on Birth Weight of Their Children. C. R. Lowe. Brit. M. J. 2:673-676 (Oct. 10) 1959 [London].

In order to obtain accurate information about smoking during pregnancy, the inquiry was limited to recent deliveries. Obstetric and smoking histories were obtained from 2,042 pregnant women delivered in 6 Birmingham maternity hospitals during the summer of 1958. It was found that the mean weight of infants of mothers who smoked regularly throughout pregnancy was 6 oz. (170 Gm.) less than that of infants of mothers who never smoked during pregnancy (6.93 lb. [3,143 Gm.] and 7.33 lb. [3,325 Gm.] respectively). This was more than the difference in weight between male and female infants and between the first and later births. It was sufficient to lower significantly the incidence of surgical induction among smokers. The effect of smoking on birth weight was unrelated to maternal

motor nerve, 1 had convulsions, 4 had sensory disturbances, and 14 had disturbances of intelligence; some of these children had several of these late sequelae simultaneously. Of these 25 children, 20 have had an extremely severe meningitis, with signs of neurological localization, poor general condition, and prolonged coma and toxic condition. The incidence of disturbances of behavior appeared to be relatively high, although they only rarely were severe enough to come within the scope of psychiatry. Most of the organic lesions found at the follow-up examination were not observed at the time of the patient's discharge from the hospital. This explains the general attitude of optimism concerning the immediate prognosis of the disease. The results of the long-term follow-up strongly suggest that the long-range prognosis of suppurative meningitis in children should be considered with more reserve, and one should be more cautious with regard to the immediate optimism of therapeutic success.

Hyperkalemic Familial Periodic Paralysis. T. J. Egan and R. Klein. Pediatrics 24:761-773 (Nov., part 1) 1959 [Sprinfield, Ill.].

The authors studied the members of 3 unrelated families who were affected by the hyperkalemic (hyperpotassemic) variant of familial periodic paralysis. Clinical histories relating to attacks were obtained directly from 11 affected persons, and indirectly on 30 others through information supplied by close relatives. The ages of the affected persons ranged from 19 months to 65 years. Five affected persons—a 32-year-old woman, a 30-year-old man, and 3 boys, aged 8, 7, and 14 years, respectively—were selected from the 3 families to be hospitalized and studied in detail. The paretic attacks in these persons were characteristically associated with elevation of concentration of potassium in the serum. In the absence of a decreased rate of urinary excretion of potassium, the cause of the increase in concentration of potassium in the plasma must have been a shift of potassium from the intracellular to the extracellular space, since the studies of total concentration of protein in the plasma did not indicate a shift of water in the opposite direction of sufficient magnitude to account for the change in concentration of potassium. During the recovery period, a shift of potassium from the extracellular to the intracellular space must occur, since an increased urinary excretion of potassium could not always account for the fall in concentrations in the plasma.

The administration of glucagon (30 mcg. per kilogram of body weight) intravenously, or of epinephrine (0.25 to 0.4 ml. of a 1:1,000 dilution of epinephrine hydrochloride) subcutaneously, during an acute attack terminated the attack promptly. The choice of these drugs for trial in therapy was determined by their effect in reducing concentration of potassium in the plasma coincident with the resulting increase in concentration of sugar in the blood. The intramuscular administration of 10 to 15 mg. of dextro amphetamine sulfate (Dexedrine Spansules) daily controlled symptoms in 2 patients, and resulted in definite improvement in a third patient treated for periods varying from 3 to 7 months. The mode of action of this drug in causing a fall in concentration of potassium in the plasma requires further investigation.

Copper and Protein Depletion Complicating Hypoferric Anemia of Infancy. W. K. Schubert and M. E. Lahey. Pediatrics 24:710-733 (Nov., part 1) 1959 [Springfield, Ill.].

The authors report on 5 male and 9 female infants, between the ages of 4 and 17 months, who were studied in the outpatient clinic or hospital wards of the Children's Hospital or the General Hospital in Cincinnati between 1955 and 1957. Medical care was sought for them because of pallor, edema, or concomitant infection. These infants had a syndrome consisting of iron-deficiency anemia, hypocupremia, and hypoproteinemia. Significant retardation of growth was noted in 7 of the 14 patients. Evidence indicated that the hypocupremia was due to copper depletion, which was suggested by the reduced concentration of copper in the serum, by the persistence of this after restoration of the serum proteins to normal, and by the prompt increase in concentration of copper in the serum after the oral administration of copper. The reduced concentration of copper in the erythrocytes of some patients, and in the liver of one patient, constituted additional supportive evidence. The existence of iron depletion was suggested by the morphologic features of the anemia, the hypoferremia, and the reduced saturation of iron-binding protein, and was confirmed by the prompt hematological response to the administration of iron that contained negligible quantities of copper. Abnormalities in the absorption and utilization of iron were not observed. The study of an additional 54 infants, most of whom were between the ages of 6 and 18 months, with iron-deficiency anemia but normal or elevated levels of copper in the serum, revealed a significant degree of growth retardation and hypoalbuminemia, both of which correlated with the severity of the anemia.

While the exact pathogenesis of the syndrome of hypocupremia, iron-deficiency anemia, and hypoproteinemia remains to be determined, the observations made by the authors in these 2 groups of infants, together with those made by other workers, can be formulated into the following brief working hypothesis. The primary defect is one of iron deficiency, arising from the combination of factors usually operative in infants, i. e., insufficient weight, age, and parity, or to the complications of pregnancy. It was not due to the shortening of pregnancy (brought about by early onset of labor). It is concluded, therefore, that smoking during pregnancy substantially retards fetal growth.

Case of Tuberculosis of the Placenta. J. W. Boesaart. Nederl. tijdschr. geneesk. **103**:1849-1852 (Sept. 12) 1959 (In Dutch) [Amsterdam].

Tuberculosis of the placenta is a stage in the development of congenital tuberculosis. The author discusses criteria that have been suggested by others as indicative of congenital tuberculosis, various opinions about the involvement of the placenta, about the birth of infants with tuberculosis to women with tuberculous endometritis, and the subsequent birth of a healthy child after the mother had been subjected to antituberculous treatment. The author himself observed a 27-year-old tertipara with a history of pulmonary tuberculosis that had been cured by treatment. During the last few months of her pregnancy she was given prophylactic treatment with tuberculostatic drugs. No disturbances occurred during pregnancy, which was followed by spontaneous delivery of a girl weighing 3,890 Gm. (8½ lb.). The puerperium took a normal course. The placenta appeared normal, but microscopic studies revealed intervillous tubercles. There was no evidence of tuberculosis in the infant, and both mother and child have remained well.

PEDIATRICS

Vascular Compression of the Trachea and Oesophagus. F. R. Edwards. Thorax 14:187-200 (Sept.) 1959 [London].

In the developing embryo the foregut is surrounded by a group of vascular structures of bilateral distribution connected with the branchial arches. Portions of these arches are obliterated to form the normal aorta and the great vessels. The ultimate persistence of only one main vascular arch, the left, as the aorta, permits the trachea and the esophagus to lie freely to its right side. Where, however, the vascular obliteration in the embryo stage is abnormal, the residual vessels may so closely surround the trachea and the esophagus that either or both become compressed, and symptoms are produced. After reviewing the early literature, the author gives a detailed and illustrated description of the embryologic development. With regard to the pathology, he says that vascular compression of the trachea and of the esophagus is produced by (1) a vascular ring and (2) a partial vascular ring, and lists the vascular structures producing these ring structures. Vascular compression of the trachea alone may be produced by levoposition of the innominate artery and dextroposition of the left common carotid artery. Vascular compression of the esophagus alone may be produced by an aberrant right subclavian artery arising as the last division of the normal aortic arch.

Compression of the trachea results in maldevelopment and softening of the cartilages and a narrowing of the lumen, some 2 to 3 cm. above its bifurcation. The walls are lax, and the pressure changes of respiration produce a stridor. The mucosa in the region of the stricture may be edematous and reddened due to persistent irritation, and considerable mucoid secretion is frequently present. The inflamed stricture acts as a cilial barrier, and secretion may accumulate below it. The lack of development of the lumen will remain if relief is not provided early. Although the lumen of the esophagus is compressed, it is unusual for a true stricture to develop. Other congenital derangements found with abnormalities of the aortic arch include hemivertebrae, spina bifida, abnormal rib formations in the upper thoracic region, pulmonary stenosis, and the tetrad of Fallot.

The author describes observations on 16 children with vascular obstruction, who were operated on. Eleven had a double aortic arch, and 5 an aberrant right subclavian artery. All the children survived the operation. Although dysphagia, when present, appeared to be relieved immediately, the stridor frequently took some months to disappear, and even then a mild stridor might be noticeable if a tracheobronchial infection occurred. It is expected, however, that in the course of time, as the trachea grows, this symptom will completely disappear. Vascular compression of the trachea and the esophagus due to abnormalities of the aortic arch and its branches produces symptoms in some 1% of all cases of congenital abnormalities of the heart and great vessels. Persistent stridor and dysphagia in infancy may be due to this condition. It can be cured by surgical division of the obstructing vessels, and a fatal outcome may be prevented. The type of constriction can be accurately diagnosed in most cases by radiographic study and endoscopy.

Long-Term Prognosis of Suppurative Meningitis in Early Childhood. M. Cavellat, Y. Delaroche and E. M. Heilmann. München. med. Wchnschr. **101**: 1733-1735 (Oct. 2) 1959 (In German) [Munich, Germany].

The authors report on 82 children with suppurative meningitis, who were admitted to the pediatric clinic of the University in Nantes, France, between 1951 and 1957. Eleven children died in the hospital; 71 children were discharged as cured. Twenty-one of the 71 children were lost to follow-up; 50 children were reexamined 6 months to 7 years after their discharge. Late sequelae were observed in 25 (50%) of the children, 6 of whom had paralysis of the extremities, 4 had paralysis of the oculomotor nerve, 1 had convulsions, 4 had sensory disturbances, and 14 had disturbances of intelligence; some of these children had several of these late sequelae simultaneously. Of these 25 children, 20 have had an extremely severe meningitis, with signs of neurological localization, poor general condition, and prolonged coma and toxic condition. The incidence of disturbances of behavior appeared to be relatively high, although they only rarely were severe enough to come within the scope of psychiatry. Most of the organic lesions found at the follow-up examination were not observed at the time of the patient's discharge from the hospital. This explains the general attitude of optimism concerning the immediate prognosis of the disease. The results of the long-term follow-up strongly suggest that the long-range prognosis of suppurative meningitis in children should be considered with more reserve, and one should be more cautious with regard to the immediate optimism of therapeutic success.

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The administration of glucagon (30 mcg. per kilogram of body weight) intravenously, or of epinephrine (0.25 to 0.4 ml. of a 1:1,000 dilution of epinephrine hydrochloride) subcutaneously, during an acute attack terminated the attack promptly. The choice of these drugs for trial in therapy was determined by their effect in reducing concentration of potassium in the plasma coincident with the resulting increase in concentration of sugar in the blood. The intramuscular administration of 10 to 15 mg. of dextro amphetamine sulfate (Dexedrine Spansules) daily controlled symptoms in 2 patients, and resulted in definite improvement in a third patient treated for periods varying from 3 to 7 months. The mode of action of this drug in causing a fall in concentration of potassium in the plasma requires further investigation.

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While the exact pathogenesis of the syndrome of hypocupremia, iron-deficiency anemia, and hypoproteinemia remains to be determined, the observations made by the authors in these 2 groups of infants, together with those made by other workers, can be formulated into the following brief working hypothesis. The primary defect is one of iron deficiency, arising from the combination of factors usually operative in infants, i. e., insufficient iron stores, inadequate intake, and excessive requirements for iron. With the gradual development of moderately severe anemia, the metabolism of protein is altered in some undisclosed fashion, but with the result that (in addition to growth retardation, edema, and hypoproteinemia), the anemia worsens—perhaps because the now superimposed protein depletion interferes further with iron metabolism or because the anemia is now compounded into one due to depletion of both iron and protein. Finally, with aggravation of the protein-deficient state, copper retention is impaired, and both blood and tissues become partially depleted of this mineral. Such a concept of the development of the complete syndrome, although not the sole possibility, seems most consistent with the reported data.

Fluorescence of the Erythrocytes in Lead Poisoning in Children: An Aid to Rapid Diagnosis. J. A. Whitaker and T. J. Vietti. Pediatrics 24:734-745 (Nov., part 1) 1959 [Springfield, Ill.].

Red fluorescence of erythrocytes occurs during lead poisoning. The authors examined microscopically with the aid of blue ultraviolet light a thin wet-preparation of erythrocytes obtained from 7 untreated children, between the ages of 15 and 36 months, with lead poisoning. In every one of these children the red fluorescence was observed in 75 to 100% of the erythrocytes. The exact nature of the fluorescent material in the erythrocytes has not been determined; it is probable that the fluorescence is related to the amount of free protoporphyrin in the erythrocytes. One hundred fifty control specimens, obtained from normal children and others with various clinical conditions, also were examined microscopically and showed 0 to 50% fluorescent erythrocytes. This test is a simple, rapid, reliable method to aid in the diagnosis of lead poisoning in children.

Favorable Response of Calcinosis Universalis to Edathamil Disodium. H. Davis and P. J. Moe. Pediatrics 24:780-785 (Nov., part 1) 1959 [Sprinfield, Ill.].

The authors report on a 12-year-old girl with calcinosis universalis, an unusual metabolic disorder of unknown causation, which is characterized by the widespread deposition of calcium salts in skin and subcutaneous tissues. The patient appeared extremely emaciated. Body movement and speech were extremely slow. There was marked wasting of muscles, with prominence of the underlying skeletal structures. Scattered over the body were areas of hyperpigmentation under which one could palpate hard gravel-like masses. During the 2 months preceding her admission to the pediatric department of the University of Texas Hospitals in Galveston, the patient's condition had been unchanged by adrenal steroid therapy or symptomatic treatment. Since the use of a calcium chelating agent appeared to offer a logical therapeutic approach, the patient was given 0.85 Gm. of edathamil disodium (Endrate) intravenously over a 4-hour period daily for 5 days of each of 3 consecutive weeks. Marked subjective improvement accompanied by rapid gain in body weight started about 10 days after the administration of edathamil disodium. The significance of this observation seemed to be enhanced by the fact that other methods of treatment, previously employed, were ineffective. The effectiveness of the edathamil disodium therapy was indicated by a decrease in ectopic calcification of the subcutaneous tissues; the skin lost its shiny appearance, and the subcutaneous nodules became less pronounced. Muscle testing showed moderate increase in strength, and joint mobility improved. A slight increase in urinary excretion of calcium occurred during the administration of the chelating agent, but it is difficult to evaluate the significance of this chemical finding. Although only slight evidence of loss of calcium from the body tissues was shown chemically, the decrease in the aberrant calcific deposits revealed by roentgenographic studies lends convincing evidence of improvement resulting from the administration of edathamil disodium. The results reported suggest the necessity for further therapeutic and chemical studies employing edathamil disodium in patients with calcinosis universalis.

Composition of Tracheobronchial Secretions in Cystic Fibrosis of the Pancreas and Bronchiectasis. W. S. Chernick and G. J. Barbero. Pediatrics 24:739-745 (Nov., part 1) 1959 [Springfield, Ill.].

The authors obtained tracheobronchial secretions by bronchoscopic aspiration from children and adolescents, between the ages of 4 and 16 years, with cystic fibrosis of the pancreas, and from adults with chronic bronchiectasis. These specimens were analyzed for the major organic and inorganic constituents. The tracheobronchial secretions from patients with cystic fibrosis contained, on a weight basis, at least twice the quantity of organic material found in bronchiectatic secretions. The results of dry weight determinations of nitrogen, carbohydrate, hexosamine, and lipids indicated that similar quantities of these organic constituents were found in the 2 types of secretions studied. The only organic component which was found to be consistently different was desoxyribonucleic acid; a higher content was found in the secretions obtained from patients with cystic fibrosis than in those from patients with bronchiectasis. Analysis of the inorganic constituents revealed a higher content of sodium and potassium in the bronchiectatic secretions, when calculated on the basis of both wet and dry weight, whereas phosphorus was found to be higher in the secretions obtained from patients with cystic fibrosis. The calcium content in the total number of specimens obtained from patients with cystic fibrosis was found to be twice that observed in those obtained from patients with bronchiectasis; however, when calculated on the basis of dry weight, both types of secretions contained similar amounts of calcium.

High molecular weight polymers are greatly influenced by the surrounding ionic concentration. In secretions from patients with cystic fibrosis, the quantity of sodium ions which are influencing the polymeric structures is less than the number affecting these structures in the bronchiectatic material. The difference in the ratio of ionic to organic constituents noted in the more viscous secretions from patients with cystic fibrosis, as compared with the less viscous bronchiectatic material, suggests the possibility that the physical differences shown in the bronchial tract could result from an alteration in the physicochemical bonding characteristics of the secretions. An alteration in the ionic concentration, which may be responsible for the peculiar characteristics observed in the tracheobronchial secretions of patients with cystic fibrosis, emphasizes the need for extensive research in this area because of the serious obstruction produced by the secretions of the tracheobronchial tree in patients with cystic fibrosis of the pancreas.

Familial Fibrocystic Pulmonary Dysplasia and Its Relation to the Hamman-Rich Syndrome. W. L. Donohue, B. Laski, I. Uchida and J. D. Munn. Pediatrics 24:786-813 (Nov., part 1) 1959 [Springfield, Ill.].

The authors draw attention to a peculiar "interstitial pneumonitis" observed in 5 infants from 3 families. These infants were admitted to the Hospital for Sick Children in Toronto and died; their ages at the time of death varied between 7 weeks and 18 months. In the first of these families with 3 affected infants, there was chronic pulmonary disease in 4 adults; in the second family one infant and one adult were affected; the only suggestion that the infant in the third family had familial cystic fibrosis of the lung was the pathological similarity of the pulmonary lesions to those of the affected infants in the other 2 families. In each of the adult patients the total picture of the disease, from data available, was identical with that of the Hamman-Rich syndrome—an idiopathic, progressive, primary pulmonary insufficiency, characterized chiefly by a diffusion defect, with clubbing of the fingers and cor pulmonale as common secondary manifestations, and with chest roentgenograms suggestive of interstitial fibrosis with varying degrees of emphysema and bullae formation. In the infants the presence of unexplained progressive pulmonary insufficiency, especially if associated with a refractory nonspecific failure to gain, was suggestive but not diagnostic. In order to distinguish these 10 cases from others included in the 87 accepted, heterogeneous cases of Hamman-Rich syndrome, which were collected from the literature, the term "familial cystic fibrosis of the lungs" or "familial fibrocystic pulmonary dysplasia" is suggested. Fourteen of the 87 cases also were familial.

In the infants, unless one is aware of the familial background of the disease, the changes appear to have been caused by infection or some obscure inflammatory reaction rather than the end-result of anatomic or physiological defect. It may possibly be that the main genetic defect is a failure of deepithelization of the alveoli and that the interstitial pneumonitis and subsequent fibrosis and cystic formation are secondary to this. It is quite obvious that, whatever the genetic defect may be, it is certainly not an all-or-none phenomenon, and there must be varying degrees of impairment of pulmonary function even in the same family. Death may occur in the first few months of life, or an affected person may reach a relatively ripe old age before eventually succumbing to the disease. In addition, obvious carriers of the abnormal gene remain healthy. The data available at present will not allow definite conclusions as to the precise mode of inheritance. The disease is probably inherited as a simple autosomal dominant gene, but until larger genealogical trees are examined in detail and male-to-male transmission is proved to occur, the possibility of sex-linked dominant inheritance should not be overlooked.

Incidence of Infection in Children After Splenectomy. B. Laski and A. MacMillan. Pediatrics 24:523-527 (Oct.) 1959 [Springfield, Ill.].

It was the impression of Laski and MacMillan that they had not observed an abnormal number of postoperative complications in children subjected to splenectomy, although since the report by King and Schumacher in 1952 regarding severe infections in splenectomized children, numerous confirmatory reports have appeared. The authors investigated the records of 81 patients who had undergone splenectomy at 2 children's hospitals in Toronto, and compared them with those of 94 children of similar age who had undergone appendectomy with regard to subsequent infections. Purulent meningitis developed in 1 child in each group, and among those who had undergone appendectomy there were 4 others who had aseptic meningitis. Thus, it would appear from this series that the incidence of serious infection in children after splenectomy is no higher than in a somewhat similar group after appendectomy.

Reviewing the literature in an attempt to correlate the disease for which splenectomy was performed with the incidence of postoperative infection, it was found that no disease was exempt, but spherocytosis seemed less likely to be followed by infection than was idiopathic thrombocytopenic purpura. However, the cases of infection reported by King and Schumacher occurred in patients with spherocytosis. It is widely believed that the spleen is one of the main sources of antibodies, but if it is not present, other tissues take over this function. Undoubtedly the spleen is a great reservoir of lymphocytes and reticuloendothelial cells, but there is much lymphoid tissue left in the body, and this is especially so in children from whom the spleen has been removed. Studies of gamma globulin have failed to reveal any deficiency in children who have undergone splenectomy. Studies of antibody response to diphtheria toxoid have shown no difference between splenectomized and nonsplenectomized subjects. The authors feel that, while they cannot ignore the findings of such careful observers as have reported this subject, they are unable to confirm their findings, and at the present time must consider splenectomy as no more hazardous than other major operations.

The Jaundice of Premature Infants. O. Tezner and J. Levi. Ann. paediat. 193:247-254 (Oct.) 1959 (In German) [Basel, Switzerland].

The authors' observations in the premature infant department of the Public Health Service in Tel Aviv, Israel, showed that the jaundice of premature infants can by neither clinical nor laboratory methods be differentiated from the physiological jaundice of mature newborn infants, and is probably identical with it. The higher incidence and the greater severity of the jaundice of premature infants seem to depend on the higher degree of immaturity of the liver. Indications for exchange transfusions should be based not only on the bilirubin content of the serum but also on the clinical aspect of the infant. Exchange transfusions should be performed primarily in premature infants with a bilirubin concentration above 18 mg. per 100 cc., but then also in premature infants whose body weight varies between 1,000 and 1,500 Gm. (2 and 3 lb.) and in whom apathy, vomiting, and apnea occur even when the serum bilirubin level is low.

There are at present 2 concepts concerning the origin of kernicterus. According to one concept, the indirect bilirubin, found by Claireaux in the nuclei, not only stains the nuclei but also damages them. According to the other concept, bilirubin stains only such nuclei as have previously been injured by other factors, such as anoxia. The authors' findings in premature infants with jaundice, in conjunction with Meyer's observations that kernicterus is not related to the bilirubin content of the cerebrospinal fluid, support the second concept.

Bacillus Subtilis Septicemia: Report of a Case and Review of the Literature. R. Cox, G. Sockwell and B. Landers. New England J. Med. 261:894-896 (Oct. 29) 1959 [Boston].

The authors present the history of a boy who was hospitalized at 2½ months of age for severe gastroenteritis, and at that time it was observed that hydrocephalus was developing. At 4½ months of age he was admitted to another hospital for a ventricular-jugular shunt procedure, which was carried out with the use of a Holter valve. For 5 months after discharge the patient did well, but then enlargement of the head again became progressive. The Holter valve was removed, and a thrombus was detected in the internal jugular vein that had occluded the distal tube. Four days later another ventricular-jugular shunt was performed. Fever developed on the day after this operation and continued despite treatment with penicillin and streptomycin.

When 2 blood cultures yielded Bacillus subtilis, the organism was at first regarded as a contaminant, but subsequent cultures substantiated B. subtilis infection. Although the patient became relatively afebrile after 8 days of treatment with antibiotics, B. subtilis continued to grow from the blood stream. Fever developed again, with temperature spikes to 105 F (40.5 C). Extreme irritability, vomiting, and lethargy developed, and antibiotics were reinstituted. Seven blood cultures and one bone marrow culture were obtained over the next 4 weeks, and all were positive for B. subtilis. On the 69th hospital day administration of massive doses of penicillin was begun intravenously. The patient received 50 million units each day for 7 days and up to 25 million units each day for the following 18 days. Kanamycin therapy had also been started intramuscularly on the 61st hospital day and was continued for 34 days, but blood cultures remained positive for B. subtilis.

When it finally became obvious that the bacilli had been originating from the valve, the valve apparatus was removed and replaced, and the patient became asymptomatic. Reviewing the literature, the authors show that infection with the B. subtilis group of organisms is much more common than is generally realized. Any organ system may be involved, but the eye is the most common site of infection.

Toilet Training and Enuresis. S. B. Dimson. Brit. M. J. 2:666-670 (Oct. 10) 1959 [London].

It has been stated that the method of toilet training is a major factor in the production of enuresis. Some investigators found that most enuretics had received insufficient training, but others incriminated coercive methods, including early training. This report is concerned with a retrospective inquiry concerning toilet training in 165 "wet" families, in which there were 225 enuretic children and 174 "dry" siblings, and in 174 "dry" (control) families with 384 children, none of whom had enuresis. The mothers of these families were questioned regarding the age at which toilet training was begun, whether it was carried out strictly or not, whether it was resisted or resented, and the ages at which bladder and bowel control were achieved, if at all. The position of the child in the family was noted, and the same questions were posed concerning the siblings if over 2 years old, since by that age complete data on control might be expected in most cases.

The age at which training ("potting") began was virtually the same in the enuretics, dry siblings, and controls (30% under 3 months, 42% between 3 and 9 months, and 28% over 9 months). It was concluded that the time of beginning training bears no relation to the problem of enuresis. Strict methods were adopted in a minority of children, but were more prevalent if training began below the age of 3 months and more common in enuretics who were first-born or "only" children; nevertheless, enuresis was found less often among those trained very early. Later-born enuretics were not trained more strictly than their dry siblings or the controls. For these reasons it is doubtful whether coercive training is an important factor in the production of enuresis. Children trained in the later period (over 9 months) were handled leniently, as a rule, but no difference in this respect was found between the enuretic and control groups, indicating that lax methods were likewise not more conducive to enuresis.

Strict training was more often associated with resistance, both active and passive, in all the children. Enuretic children resisted much more often than the controls, even if training had been lenient; most resistance was observed when training began after 3 months of age. It is inferred that this resistance is more closely related to enuresis than early training, but coercive methods played some part in producing it. Early training seemed to lead to earlier sphincter control, but if resisted at any training period, some delay occurred not only in enuretics but in dry children as well. The author concludes that, while toilet training has no fundamental bearing on the causation of enuresis, resistance to training is often a contributory factor.

Treatment of Bone and Joint Tuberculosis in Children. D. M. Bosworth. J. Bone & Joint Surg. 41-A:1255-1266 (Oct.) 1959 [Boston].

The growth factor plays an important role in children who require treatment for bone and joint tuberculosis. A second important factor which alters the orthopedic treatment of children, as compared with the treatment of adults, is the tendency to repair inherent in children's tissues. This capacity for spontaneous repair is separate from the growth potential; yet frequently the two seem to combine to produce favorable results. The influence of both of these factors must be taken into consideration in treating children. After discussing the destructive lesions encountered in bone and joint tuberculosis in children and the difficulties of visualizing the extent of involvement, the author shows that there has been a complete reversal of the order in which the various modes of treatment are used.

Medical treatment, with iproniazid as the drug of choice, now comes first. Time is gained by iproniazid therapy, and, in addition, there is a possibility that tubercle bacilli within the patient's organism will be destroyed, although this has not been definitely proved. Then come the so-called general measures—nutrition, rest, splintage of parts, reduction of psychic stress, and general physical care of the patient. That once resounding word "heliotherapy" is hardly ever heard. The fact that surgery comes last does not belittle its usefulness, but medical therapy and general measures have provided time and have improved the patient's condition, so that surgical treatment can be carried out with greater promise of success. This order of therapeutic measures also provides a safe period of delay, so that the growth and repair processes of childhood can become effective.

ENDOCRINOLOGY

An Attempt to Inhibit Synthesis of Corticosteroid Hormones by Means of Diethylstilboestrol in a Case of Cushing's Syndrome: Preliminary Report. N. Kovacic. Acta med. scandinav. 164:455-461 (no. 6) 1959 (In English) [Stockholm].

All signs and symptoms of adrenal cortical hyperfunction (Cushing's syndrome), as well as hyperplasia of the adrenals, disappeared in a 23-year-old woman after she had been treated with a daily dose of 5 mg. of diethylstilbestrol for several months at the medical school, University of Zagreb, Yugoslavia. Urinary 17-ketosteroids decreased to normal values as early as 3 weeks after treatment had been established, whereas normal values of eosinophilic leukocytes were reached only after 3 months of treatment, simultaneously with the disappearance of the clinical signs of Cushing's syndrome. The inhibition of synthesis of corticosteroid hormones was not complete, because the patient did not have any symptoms of hypoadrenocorticism. The administration of daily doses of 100 I. U. of adrenocorticotropin combined with daily doses of 5 mg. of diethylstilbestrol for the period of 10 days provoked higher values of 17-ketosteroids in the urine than those observed before diethylstilbestrol treatment was started, and the eosinophilic leukocytes disappeared from the peripheral blood. Eight days after the adrenocorticotropin treatment had been discontinued, the values of both 17-ketosteroids in the urine and eosinophilic leukocytes in the blood returned to normal. The administration of a daily dose of 5 mg. of diethylstilbestrol did not suffice to prevent completely the synthesis of corticosteroids.

Present Status of Endocrine Influences Upon the Stomach and Their Relationship to Peptic Ulcer Disease. S. J. Gray. Gastroenterology 37:412-420 (Oct.) 1959 [Baltimore].

A hormonal phase of gastric secretion mediated through the adrenal cortex to the stomach by way of the hypothalamus and pituitary gland was postulated by the observations of other workers; they noticed in man an increase in gastric hydrochloric acid and pepsin secretion during prolonged corticotropic hormone stimulation unaffected by vagotomy but requiring an intact adrenal gland. It was suggested that chronic emotional and physical stress might be transmitted to the stomach by a hormonal pathway through the hypothalamic-pituitary-adrenal mechanism, independent of the vagus nerve and gastric antrum, and that acute or chronic peptic ulcer might be induced in man through this purely hormonal mechanism. The gastric secretory response to adrenal stimulation was determined by measuring the gastric acid and pepsin secretion during the administration of corticotropin or the adrenal steroids. The results showed that the adrenal steroids appear to increase gastric acid and pepsin in man and in animals, increase the tissue, plasma, and urinary pepsinogen, decrease the mucous protective barrier, and interfere with tissue repair.

Observations on patients with endocrine disease revealed that an intact adrenal gland is essential for normal uropepsin excretion. The exceedingly low levels found in patients with adrenal cortical hypofunction (Addison's disease) and hypopituitarism, and the high values associated with adrenal and pituitary hyperactivity, further emphasize the significance of adrenal influences on the stomach. Extravagal influences through the hypothalamic-pituitary-adrenal gastric pathway are demonstrable by the production of focal hemorrhages and ulcers in the stomachs of dogs similar to those produced with the vagi intact following experimental lesions in the hypothalamus and brain stem, after bilateral vagotomy.

If increased adrenal activity plays a role in the production of peptic ulcer, one might anticipate an increase in the blood and urinary corticoids. Observations on 75 normal persons and on 75 patients with duodenal ulcer showed that the concentrations of adrenal corticoids in the blood and urine of patients with peptic ulcer were not elevated, although increased adrenal activity before the development of the ulcer cannot be excluded. When a minimal adrenal stimulus was given in the form of 0.25 mg. of corticotropin (ACTH) administered intravenously in one hour, the increase in the blood hydroxycorticosteroid levels appeared to be definitely greater in patients with active duodenal ulcer than in normal persons of comparable age and sex. If patients were given a maximal adrenal stimulus, however, such as 20 mg. of ACTH intravenously over an 8-hour period, the blood hydroxycorticosteroid response was the same in the patients with ulcers as in normal persons. These data suggest that the adrenal gland of the patient with peptic ulcer may be more sensitive to a minimal stimulus than that of the normal person, as reflected by the blood hydroxycorticosteroid response. In a collected series of 1,361 patients on adrenal steroid maintenance therapy, peptic ulcer was found in 7.1%, as compared with a reported annual incidence of spontaneous development of ulcer of 0.15 to 0.38% in the general population. In a collected series of 363 patients with Addison's disease, chronic peptic ulcer was found in only 3 patients. Although peptic ulcer is extremely rare in patients with Addison's disease, chronic duodenal or gastric ulcers developed in 7 patients in the course of maintenance therapy with 12.5 to 25 mg. of cortisone given daily for 2 or 3 years. In an additional patient who had bilateral adrenalectomy, a peptic ulcer developed, with massive fatal hemorrhage, 2 years after treatment with 37.5 mg. of cortisone daily.

The adrenal hormone is presumably essential for normal gastric secretory activity, without which peptic ulcer does not occur. In the presence of excess adrenal hormone, however, the gastric and duodenal mucosa might be sensitized and excessively responsive to ulcerogenic influences which ordinarily could not induce ulceration, in accordance with the "permissive" concept of adrenal action. Hyposecretion itself may be a reflection of this increased gastric sensitivity to excess adrenal hormone. The adrenal steroids, moreover, may potentiate vagal influences on the stomach, or the adrenal gland of the patient with peptic ulcer may be more sensitive to stimulation, with a resultant exaggerated adrenal or gastric response.

The Syndrome of Congenital Goiter with Butanol-Insoluble Serum Iodine. L. J. De Groot and J. B. Stanbury. Am. J. Med. 27:586-595 (Oct.) 1959 [New York].

The authors report on 3 female patients, between the ages of 10 and 28 years, and 2 male patients, aged 15 and 17, whose cases are illustrative of one of several distinct inborn errors of metabolism responsible for sporadic congenital cretinism with goiter. The patients had goiter within the first few years of life and were definitely hypothyroid. Three of them had a familial incidence of thyroid disease. Each patient had an increased radioiodine (I^{131}) uptake by the thyroid, and all had normal or low protein-bound iodine values at the time studied. All released a significant quantity of butanol-insoluble I^{131} into the serum. Butanol solubility of the abnormal serum component was increased by chymotrypsin digestion, and in one patient it was possible to detect iodotyrosines and iodothyronines released by this digestion. When tested, deiodinase activity and serum thyroxin-binding protein were normal. Potassium thiocyanate did not release I^{131} from the thyroids. A significant proportion of urinary iodide was present as an unidentified butanol-insoluble component, probably a polypeptide, since it was dialyzable in the patients tested. In these patients, the hypothyroidism responded to standard doses of desiccated thyroid. In each of the patients, hormone replacement therapy prevented further growth of the goiter or caused marked reduction in its size. Biopsy specimens of thyroid tissue which were obtained from 2 patients showed extreme hyperplasia. In none of the patients did malignancy develop. Four additional cases, almost certainly fitting the syndrome observed in the 5 patients, were collected from the literature.

The syndrome of congenital goiter with the presence in the serum (and sometimes in the urine) of an iodinated polypeptide or protein, which is incompletely extractable from acidified serum by *n*-butanol, may be the expression of a congenital defect in thyroglobulin synthesis. It is not clear whether the iodinated polypeptide or protein is a normal or an abnormal intermediate in the biosynthesis of thyroglobulin. In any event, presumably as the result of innate deficiency of a necessary synthesizing enzyme, thyroglobulin is insufficiently elaborated, and hypothyroidism results. Similar observations in certain patients with adenomatous colloid goiter suggest that this type of congenital goiter and a type of adenomatous colloid goiter may represent different levels of expression of a common genetic defect. The clinical symptoms and signs respond to administration of desiccated thyroid, which should be instituted early in life to prevent permanent physical and mental retardation.

Liver Disease and Virilism. W. H. Smith. M. J. Australia 2:484-485 (Oct. 3) 1959 [Sydney].

Gynecomastia and diminution of facial and body hair are found commonly enough in men with liver disease, but the literature has few reports on virilism in women suffering from hepatic disease. The author presents observations on 3 young women in whom amenorrhea and virilism appeared as a prominent feature of liver disease. Two of the 3 patients, a 16-year-old girl and a 33-year-old woman, died. Although pathological confirmation of the diagnosis was not obtained, there is good evidence that the illnesses of these 3 young women were caused by hepatic disease. The most striking feature was the evidence of virilism, with failure of development of secondary sexual characteristics in one case, amenorrhea and hirsuties of masculine distribution in 2 cases, and clitoral enlargement in one. Amenorrhea and the other manifestations of virilism preceded the usual symptoms of liver disease, except in one case.

In the first case an illness resembling acute viral hepatitis with jaundice preceded the more florid aspects of the illness, although a history of excessive bleeding and possible nevi antedated this episode. In the other 2 cases no history suggestive of an attack of acute hepatitis was obtained, and most of the cases described by other observers had an insidious onset with no apparent history of acute hepatitis. Pathological study by Bearn disclosed a coarsely scarred liver, differing from the more finely hobnailed liver of Laennec's cirrhosis, with large nodules of hyperplasia, such as have been found as a sequel of viral hepatitis. Other features unusual in cirrhosis of the liver were a healthy appearance and good nutrition or even obesity. The association of amenorrhea, hirsuties, obesity, acne, and, less commonly, abdominal striae invites a comparison with adrenal cortical hyperfunction (Cushing's syndrome).

Sequential Analysis in the Assignment of Chromosomal Sex by Means of Nuclear Chromatin Patterns in Smears of Oral Mucosa. E. G. Olmstead. Am. J. Clin. Path. 32:346-349 (Oct.) 1959 [Baltimore].

Although observed in greatest numbers in the cells of females, the sex chromatin mass (or body similar to the sex chromatin mass) is also seen in the cells of males. Various distributions have been given for the percentage of sex chromatin masses in the oral mucosal cells of males and females. In any patient, the assignment of chromosomal sex may be accomplished by means of counting 100 resting cells from oral mucosal scrapings and determining the percentage of cells with sex chromatin masses. If a large percentage of cells have the sex chromatin mass, the chromosomal sex of the patient may be determined merely by scanning the slide; however, in those males who have sex chromatin masses and in those females who have few sex chromatin masses, the task of counting the chromatin-positive cells is more time-consuming. With the development of sequential analysis, it has been possible to reduce the number of observations without increasing the probability of error over the classic statistical methods.

In the present study of 100 apparently healthy students, smears were made by scraping the oral mucosa with a metal spatula and transferring the scrapings to slides coated with Mayer's albumin. These were immersed in Papanicolaou fixative for 2 to 24 hours, and then stained with cresylecht violet. Cells in the resting state were examined under oil immersion, and the sex chromatin mass was counted only when it lay against the nuclear membrane. Fifty-one males were examined by the above sequential method. The correct assignment as to chromosomal sex was determined in each instance. The number of cells examined per slide, to determine if the subject were male, ranged from 27 to 45, with a mean of 31.3 ± 6.60. The sequential table shown demonstrates that, if the first 27 resting cells examined on a slide do not contain a sex chromatin mass, the patient is male. Of the 51 males studied, 34 were assigned as males after examining only the first 27 resting cells. Forty-nine females were examined by this method. The decision that the patient was female was made after counting from 5 to 52 cells per slide, with a mean of 18.0 ± 12.4. The use of sequential analysis results in a reduction of approximately 75% in the number of oral mucosal cells required for examination in order to arrive at the correct assignment of chromosomal sex.

OPHTHALMOLOGY

Correction of Uniocular Aphakia by Means of All-Acrylic Anterior-Chamber Implants: Review of 100 Cases. D. P. Choyce. Brit. M. J. 2:609-612 (Oct. 3) 1959 [London].

Perceiving the possibilities of intraocular implant surgery (first described by Ridley in 1951), and in an attempt to avoid some of its disadvantages, other investigators, such as Strampelli, evolved an implant placed in front of the iris and behind the cornea, with feet wedged in the anterior chamber angles and carrying a central optical portion, the correction of which could be modified to suit the requirements of the individual case. This type of implant can, and indeed should, be inserted after the eye has made a satisfactory recovery from cataract surgery, thus reducing the surgical trauma inflicted upon the eye. Uniocular cataract or aphakia is common. Attempts to use a normal eye with an aphakic one by means of spectacles usually fail because of aniseikonia amounting to about 30% in most cases. A contact lens in the aphakic eye will reduce this disparity in image size to about 10%, but many patients cannot tolerate even this amount of aniseikonia. An anterior-chamber implant will reduce this figure to about 3%, which can be tolerated by the patient.

The main part of this report is concerned with 100 cases of uniocular aphakia treated with anterior-chamber implants at the Southend General Hospital, Essex. Most of these patients were unsuitable for treatment with contact lenses, because they were too young or too old, or because they had been given trial fittings and had been found to be liable to diplopia, or because they had given them up because they could not tolerate them. A modified Strampelli type of implant was used. These implants have an inner radius of curvature of 14 mm., which provides for a clearance between the central part of the posterior corneal surface and the anterior surface of the implant of between 1.5 and 2 mm. Therefore, if the implant has been correctly inserted, it is nowhere in contact with the corneal endothelium. The London manufacturers supply the implants in various sizes, and the surgeon can choose an implant of exactly the right length at the time of operation. The unused implants are returned. Some reaction was observed in the eyes of the first 30 implants. This problem seems to have been overcome by Ridley who evolved a simple method of sterilizing these implants with caustic soda. This method has been used in the subsequent 70 cases with less postoperative reaction than with the earlier cases.

Thirty-two of the 100 patients had traumatic aphakia, most of the remaining number had senile cataract, and 5 had congenital cataract (ages from 2 to 4 years). The immediate results in the first 100 cases are regarded as satisfactory. Another 5 to 10 years must elapse before the long-term results can be accurately assessed. In the meantime, this operation can be offered with reasonable confidence to persons with uniocular aphakia, who are worried by their disability and are anxious for treatment.

Tumors of the Brain Stem with Special Reference to Ocular Manifestations. P. C. Bucy and J. E. Keplinger. A. M. A. Arch. Ophth. 62:541-554 (Oct.) 1959 [Chicago].

The authors report on 105 patients with intrinsic tumors of the brain stem, whose cases were collected from the literature. Ninety-one patients were aged less than 20 years, and 46 of these were children between the ages of 5 and 4 years, i. e., a peak incidence of 43.5%. A survey of the 105 patients showed that intrinsic tumors of the brain stem are usually gliomas of various types. They most commonly involve the pons but may extend upward or downward from there. Ocular disorders, particularly paralysis of the external rectus muscles and of conjugate lateral movements of the eyes, are among the commonest manifestations. Involvement of the 3rd cranial (oculomotor) nerve usually appears late, if at all, and is usually incomplete, producing only pupillary disturbances and a partial ptosis. Exceptions are those less common cases in which the tumor arises in the midbrain rather than in the pons. Other cranial nerves, particularly the facial (7th), trigeminal (5th), auditory-vestibular (8th), glossopharyngeal (9th), and vagus (10th), are commonly involved. Increased intracranial pressure with papilledema is not uncommon, but usually develops late in the course of the disease. The descending motor pathways and cerebellar connections are almost always affected, but sensory changes in the trunks and extremities are almost never observed.

Headache, nausea, and vomiting are common complaints. The anorexia and, in addition, the common difficulty in swallowing frequently produce an emaciation of the patient. Gliomas of the brain stem usually are disorders found in patients aged less than 20 years. Symptoms suggestive of such a tumor in an adult should be investigated most carefully. They may be due to a benign removable tumor, such as a meningioma, or to some other less common disorder. There are numerous conditions which may occasionally involve the brain stem and have to be considered in differential diagnosis.

The Pupillary Membrane in Premature Infants. B. Gans. Arch. Dis. Childhood 34:292-297 (Aug.) 1959 [London].

During the last 3 years the eyes of 270 prematurely born infants were examined in the premature baby unit of Lewisham Hospital, London. The well-known difficulty of obtaining a good view of a premature infant's fundus oculi is due, in part, to the vessels of the pupillary membrane. On naked-eye examination this structure is seen as a delicate blue-gray veil behind the pupillary aperture. After homatropin mydriasis, the vessels constituting the membrane can be observed through the +20 lens of an ophthalmoscope; they form a spider's web which stands out black against the red retinal light reflex. To obtain a good view, the examiner should hold the ophthalmoscope in his right hand and the infant's head in his left, using his left index finger to retract the upper lid. A nurse holds the baby's body and retracts the lower lid with her free index finger. Care must be taken not to let the cornea become dry by prolonged examination.

The author found that the presence of a pupillary membrane, particularly if it is extensive, is a good, though nonspecific, sign of immaturity. An easily seen membrane is present in the majority of immature babies, and almost always in those weighing less than 1,500 Gm. (3 lb., 5 oz.). The number and size of the vessels closely parallels the degree of immaturity. The rate of vascular obliteration and disappearance of the membrane follows closely the infant's general progress. The author was unable to confirm Schmöger's (1955) observation on a clear-cut inverse relationship between the extent of the membrane and the length and weight of the premature infant, in that some small, but relatively mature, infants had no membrane. He also found that no hard-and-fast rule can be made about the time taken for the vessels to disappear. Most infants are discharged from the unit for premature babies when they weigh 2,721.5 Gm. (6 lb.), and in none of those discharged was a persistent pupillary membrane found.

Postoperative Infections in an Ophthalmologic Hospital: With Comments Upon Bacteriophage Typing of Staphylococci as a Preventive Tool. R. P. Burns. Am. J. Ophth. 48:519-526 (Oct.) 1959 [Chicago].

This report is based on 8,038 operations performed at the institute of ophthalmology of the Presbyterian Hospital, New York, between Jan. 1, 1956, and Dec. 1, 1958. It was found that 11 patients (0.14%) had had postoperative eye infections. There was a marked preponderance of infection due to Staphylococcus aureus, which was found on pure culture in 8 patients, while a mixed staphylococcic infection occurred in the remaining 3. The organism was antibiotic sensitive in 5 patients; it was resistant to most, or all, antibiotics tested in 5; and sensitivity tests were not made in 1. Age and general condition did not seem to be a predisposing factor to infection in this series of 11 patients. In one patient with diabetes, however, corneal abscess and hypopyon developed after cataract extraction. It is of interest that 6 of the 11 postoperative eye infections occurred in ward patients. The increased incidence of postoperative infection in ward patients has been noted before and implies a number of factors in addition to bacterial cross-contamination from large numbers of occupants; among these are prolonged illness, poor physical health, depressed economic status, suboptimal nutrition, and neglected hygiene.

Errors of technique and judgment during the operation can rapidly lead to infection with disastrous results. Vigilant care must be exercised to avoid infection. Apart from professional personnel failure, the commonest factors in postoperative eye infection were "weak ocular tissue" and multiple operations. In such patients consideration should be given to vigorous prophylactic antibiotic treatment, to spare tissue of excessive trauma, and to avoid nonabsorbable suture and foreign body implantation. Since postoperative eye infection due to Staph. aureus is a frequent occurrence in ophthalmology, and is usually antibiotic resistant, immediate treatment with kanamycin, ristocetin, or vancomycin is recommended, rather than awaiting laboratory tests for antibiotic sensitivity. When the infection is primarily due to excessive tissue trauma, congenitally poor ocular tissue, or an implanted foreign body, the choice of antibiotic is of much less importance.

INDUSTRIAL MEDICINE

Fatal Nephropathy During Edathamil Therapy in Lead Poisoning. H. G. Brugsch. A. M. A. Arch. Indust. Health 20:285-292 (Oct.) 1959 [Chicago].

In an attempt to analyze available reports in regard to possible toxic effects of edathamil calcium-disodium (Calcium Disodium Versenate) given to patients with lead poisoning, 4 cases of fatal toxic nephrosis were collected from the Swiss literature. The first patient, a 38-year-old smelter with an acute exacerbation of chronic lead poisoning, had been given excessively high doses of the drug (600 mg. per kilogram of body weight) intravenously daily for 5 days. The second patient, a 60-year-old worker with white lead, had recurrent attacks of lead poisoning and was given 3 courses of edathamil therapy, the first with a total dose of 10 Gm., the second with a total dose of 63 Gm. given within 30 days, and the third with a total dose of 17.5 Gm. The third patient, a 53-year-old painter with recurrent acute attacks of plumbism, was given 2 Gm. of the drug by intravenous infusion for 4 days (total dose, 8 Gm.), and the fourth patient, a 52-year-old man with a history of lead intoxication, received 2 Gm. by intravenous infusion for 6 days. All the patients died, and autopsies were performed on 3. Severe tubular necrosis in the area of the proximal tubules and Henle's loops, accompanied by a marked degree of cellular vacuolation and deposit of eosinophilic-staining amorphous material, were observed in 2 patients, while hyaline casts within the tubuli were observed in the third patient.

Edathamil calcium-disodium is still a good drug to be used when needed, but, as in so many recently introduced drugs, the time may not be too distant when a safer chelating agent will be substituted. Edathamil should be given only with proper evaluation of the patient's renal status before, during, and after therapy. This should include a renal function test (phenolsulfonphthalein and concentration-dilution), nonprotein nitrogen or blood urea nitrogen determinations, and at least 2 examinations of urinary sediments at the beginning of therapy and repeated whenever necessary. Courses of therapy by slow intravenous infusion should be short (probably not more than 3 days), widely spaced (more than 2 weeks apart), and with a daily total dose not to exceed 2 Gm. in adults.

Results of Treatment of Pneumoconiosis Complicated by Tuberculosis. J. H. Ramsay and A. Pines. Brit. M. J. 2:345-348 (Sept. 5) [London].

The authors present a report on 25 patients with pneumoconiosis complicated by tuberculosis, who ranged in age from 44 to 79 years and who were admitted to 3 Scottish hospitals between 1953 and 1958. Eighteen of the 25 patients had progressive massive fibrosis. Anthracotuberculosis was present in 17 of them, and silicotuberculosis in the remaining 8. Tubercle bacilli were cultured from the sputum in each case. The duration of exposure to dust ranged from 16 to 63 years. All the patients were hospitalized for from 1 to 12 months. Initial treatment consisted of 1 Gm. of streptomycin daily, with 15 to 20 Gm. of PAS and 200 mg. of isoniazid daily. When full sensitivity of the organisms was proved, the dose of streptomycin was reduced to 1 Gm. 3 times weekly. Once the sputum had become persistently negative on culture, the patient's discharge from hospital was considered. Ambulatory treatment with combined cachets of PAS of 5 Gm. twice daily and 100 mg. of isoniazid twice daily was continued. As there are usually open cavities left in these patients, a minimum of 2 years of continuous chemotherapy was given.

In all 25 patients sputum conversion to negative occurred within 1 to 8 months from the time treatment was started, except in 1 patient who did not cooperate and subsequently had a relapse. Four of the 25 patients died of nontuberculous causes. Thirteen patients who have completed chemotherapy have remained culture-negative for periods ranging from 1 to 37 months after treatment was stopped. There has been slight radiographic resolution in more than half of the patients, but cavity closure was obtained in only one patient with progressive massive fibrosis. It is believed that the reason for any failure reported in the treatment of pneumoconiosis complicated by tuberculosis has been the incorrect use of chemotherapy. The normal principles of antituberculous chemotherapy should apply in the same way, whether pneumoconiosis is present or not.

THERAPEUTICS

Long Term Anticoagulant Therapy: A Six-Year Study of an Indandione Derivative. W. B. Rawls and C. A. R. Connor. Am. J. Cardiol. 4:470-475 (Oct.) 1959 [New York].

The authors report on 300 patients who received long-term anticoagulant therapy with phenindione (Hedulin). Of these patients, 100 with some form of peripheral vascular disease or myocardial infarction were hospitalized at St. Clare's Hospital in New York, and 200 who had recovered from acute attacks of thrombophlebitis, myocardial infarction, and other thromboembolic disorders were ambulatory. In hospitalized patients, in whom the prothrombin time was determined frequently, large doses of phenindione, 300 to 400 mg. the first day and 200 to 300 mg. the second day, were given to obtain quick results. The full therapeutic effect was attained within a short time, and in most instances the prothrombin time returned to normal within 48 hours after the medication was omitted. The average maintenance dose necessary to maintain the prothrombin at a good therapeutic level (2 to 2½ times the control) varied between 50 and 100 mg. daily. In the ambulatory patients, the prothrombin times were determined every 1 to 3 weeks. When the maintenance dose was established, the prothrombin time did not fluctuate widely, and, therefore, it was not necessary to repeat the prothrombin tests often, and administration of the drug could be continued with a great degree of safety.

Hemorrhage occurred only twice in this series of patients—once when a patient had a tooth extracted without the knowledge of the authors while receiving phenindione, and once when a patient inadvertently increased the dose of the drug to 2½ times the prescribed dose. When hemorrhage occurs, it can be controlled by the withdrawal of the drug and the use of vitamin K_1, and the prothrombin time rapidly returns to a normal level. Phenindione proved useful in both hospitalized and ambulatory patients.

Further Observations on Flumethiazide: A New Oral Diuretic Agent. T. Bodi, M. Fuchs, S. Irie and J. H. Moyer. Am. J. Cardiol. 4:464-469 (Oct.) 1959 [New York].

The authors report on 8 women, between the ages of 37 and 73 years, with cardiac disease, selected from the wards of the Hahnemann Hospital in Philadelphia, in whom the effect of flumethiazide (an orally administered saluretic agent of the sulfamyl benzothiazide group of chemical compounds) on renal hemodynamics was studied. Seven of the 8 patients were given 800 mg. of flumethiazide orally, and one of these received also 2,000 mg. of the drug orally one week later. The 8th patient received a trial dose of 1,000 mg. given intravenously within 20 minutes. Glomerular filtration rate and renal plasma flow were not altered when doses not exceeding 2,000 mg. were given. The electrolyte excretion of 16 patients with compensated arteriosclerotic heart disease and without gross renal functional derangement was studied during 6 days of administration of flumethiazide. Five of the 16 patients were given 800 mg. of the drug twice daily, 5 patients received 1,000 mg. twice daily, and 6 patients were given 1,000 mg. daily for 6 days. The results showed that the main effect of flumethiazide is on sodium, chloride, and water excretion. Significant effects on potassium excretion were not observed. The maximum effect of continuous daily administration was reached within the first 2 days, and this was followed by gradual return of natruresis to the control level within 4 to 6 days.

No unpleasant effects were noted when the single dose did not exceed 1,000 mg. Nausea and gastric discomfort were noted after giving a single dose of 2,000 mg. to 2 patients of advanced age. This was eliminated promptly by reducing the dose to 1,000 mg. given twice a day. The therapeutic efficiency and the minimal kaliuretic effect make flumethiazide a valuable addition to the armamentarium for the management of patients with edema.

Digitalis Delirium: A Report on Three Cases. G. Church and H. J. L. Marriott. Circulation 20:549-553 (Oct.) 1959 [New York].

The authors report on 3 men, between the ages of 57 and 83 years, with congestive heart failure, who were treated with 3 different digitalis preparations at the Mercy Hospital in Baltimore and in whom delirium resulted from digitalis intoxication. The 3 preparations administered to these patients were gitalin, digoxin, and digitoxin. In the 83-year-old man delirium occurred as the earliest convincing manifestation of intoxication with digitoxin. Previously gitalin and digoxin pushed to early toxicity had not produced mental symptoms, and subsequently digitoxin itself did not reproduce it. The case of this patient thus showed that the signs of early intoxication in a single patient may vary with different preparations and indeed with the same glycoside on separate occasions. In the 57-year-old man the alarming feature was the more than 14-day duration of the digitalis delirium which occurred with 1.5 mg. over the minimal intoxicating dose of digoxin. Manifestations of intoxication with the short-acting glycosides usually disappear within 48 hours, but exceptions do occur. It is of further interest that delirium persisted in this patient long after other signs of intoxication, such as anorexia and blurring of vision, had disappeared.

In the third patient, a 65-year-old man, delirium occurred in the presence of other possible causative agents besides digitalis. Severe infection, hepatic failure, uremia secondary to renal failure, and electrolyte imbalance could have been responsible. As the delirium became worse, however, tests of hepatic function improved, and the urea level fell; moreover, little or no increase in the patient's urinary output coincided with the dramatic improvement in his symptoms, which occurred when gitalin was withheld. The evidences of severe infection developed and disappeared before his delirium reached its peak, and the low-grade pyrexia, which developed later, persisted after improvement had occurred. Electrolyte imbalance was possibly present, but, considering the progression, the associated gastrointestinal disturbances, and the bigeminy, the weight of evidence appears to incriminate gitalin. The case of this patient illustrates how easily the diagnosis of digitalis intoxication can go unrecognized when superimposed on a complex clinical picture. Several clinical features, previously noted by other observers, also were seen in these 3 patients, namely, the frequent association of the delirium with lesions of the aortic valve; the commoner occurrence in older age groups; variation in the type of psychosis with the personality of the patient; its occasional occurrence as the earliest and possibly the only sign of intoxication; and its occurrence in the absence of electrolyte changes, administration of sedatives, Cheyne-Stokes respiration, and anoxia.

Clinical Experience With Chlorpropamide in Diabetes. L. L. Pennock. Pennsylvania M. J. 62:1537-1539 (Oct.) 1959 [Harrisburg].

The author reports on 118 selected patients (68 women and 50 men) with diabetes mellitus, who were treated with chlorpropamide for periods varying from 6 to 14 months; the majority of the patients were over 40 years of age. Of the 118 patients, 95 showed excellent control of their diabetes on doses of 250 mg. once or twice daily. Chlorpropamide also proved to be successful in smaller doses in the treatment of a number of patients. The condition of these patients was either poorly controlled on tolbutamide, or they had experienced secondary failure with tolbutamide. Side-effects from chlorpropamide were transient and mild in this group of patients. Laboratory tests showed no effect on blood urea nitrogen level, thymol turbidity reading, or blood counts. Hypoglycemia was not experienced after the dose of the drug was reduced.

Chlorpropamide should be used only in the treatment of stable, nonketotic adult diabetics whose diabetes was found after the age of 40. Dietary control is essential for the treatment of all diabetics and chlorpropamide need not be used when diet alone is adequate.

Clinical Experience With Chlorpropamide. A. J. Finestone and R. Minsek. Pennsylvania M. J. 62:1539-1541 (Oct.) 1959 [Harrisburg].

The authors report on 63 selected patients with diabetes mellitus, who were treated on an outpatient basis with chlorpropamide given orally since April, 1958. None of the 63 patients have been followed up for less than 8 months, and 32 of them were followed up for 1 year or longer. Treatment with chlorpropamide showed good results in 39 patients, i. e., the fasting blood sugar level was generally under 150 mg. per 100 cc. in these patients, and they felt clinically well. None of these 39 patients required more than 500 mg. of the drug, and 20 of them required doses of less than 250 mg. Fair results were obtained in 11 patients. Control in these 11 patients was equal to, or better than, that with insulin or tolbutamide therapy, but their fasting blood sugar level did not fulfill the definition for a "good" control. There were 9 failures in this series of patients. Only one of these was obese. Six of these 9 patients had received less than 40 units of insulin daily before therapy with chlorpropamide was started. Chlorpropamide appears to be a satisfactory agent in selected patients for the oral therapy of diabetes mellitus, but the criteria for the selection of patients who will respond to this therapy have not been ascertained.

Moniliasis of Lung Treated with Amphotericin B. A. Videbaek and K. R. Eriksen. Ugesk. læger 121:1528-1530 (Oct. 1) 1959 (In Danish) [Copenhagen].

In a man, aged 52 years, with chronic lymphogenous leukemia, high continuous fever suddenly set in, with marked headache, cough, auscultatory and roentgenologic signs of pneumonia on the left side, and pronounced hemolysis. Many yeast cells were found in the sputum. Penicillin was without effect. After the oral administration of prednisone for 12 days and of 50 mg. of amphotericin B intravenously for 8 days, the number of yeast cells in the expectorate decreased rapidly, the temperature became normal, and the auscultatory changes slowly receded. The difficulty in examining the sputum is stressed. Microscopic demonstration of cells from the bronchi and alveoli is necessary to assure that the expectorate originates from the lungs.

Fatal Amebiasis Complicating Corticosteroid Management of Pemphigus Vulgaris. J. Eisert, J. E. Hannibal Jr. and S. L. Sanders. New England J. Med. 261:843-845 (Oct. 22) 1959 [Boston].

The authors report a case of fatal amebiasis developing during the course of corticosteroid therapy for pemphigus vulgaris. The presence of latent amebiasis and its possible activation through the administration of corticosteroids should be considered when one is confronted with unexplained diarrhea in a patient treated with these agents.

Immediate Diuretic Effects of Hydrochlorothiazide (Esidrex). P. Borba, J. Scherb and G. T. Henriques. Hospital 56:489-498 (Sept.) 1959 (In Portuguese) [Rio de Janeiro].

Fifty patients hospitalized at the therapeutic clinic of the University of Recife and at the Hospital Centenario in Recife, Brazil, were treated with hydrochlorothiazide. The patients were divided into 4 groups, each group containing some edematous and some nonedematous subjects. Four therapeutic approaches were used: (1) administration of one dose only of 50 mg. of hydrochlorothiazide; (2) one dose only of 100 mg.; (3) administration of a daily dose of 50 mg. during 3 consecutive days; and (4) a daily dose of 100 mg. during 3 consecutive days. Evaluation of the effects, when the therapy consisted of one dose only, was made by comparing the average diuresis of the 3 days preceding the therapy with the average diuresis within 24 hours after the administration of hydrochlorothiazide and during the 3 subsequent days. When the drug was administered during a period of 3 consecutive days, the diuretic effects were evaluated by comparing not only the average but also the daily urinary output of the 3 days preceding the therapy, of the next 24 hours, and of the next 3 days.

Ten patients received one dose only of 50 mg. of hydrochlorothiazide. The average urinary output, which was 911.8 cc. during the 3 days prior to the medication, increased to 1,633 cc. in the next 24 hours and dropped to 824.6 cc. during the 3 subsequent days. The diuretic increase was approximately the same in both the edematous and the nonedematous patients, although the gross volume of diuresis was greater in the edematous. Seven patients received a daily dose of 50 mg. during 3 consecutive days. The average diuresis went from 945.5 to 1,496 cc., then decreased after the third day. Eleven patients received 100 mg. of hydrochlorothiazide daily during 3 days. The average diuresis increased from 837 to 1,454 cc., dropping to 855 cc. during the 3 days after the therapeutic period. The therapeutic effects in these 2 groups of patients were again more marked, and the subsequent drop in diuresis was less pronounced in the edematous than in the nonedematous patients. The authors interpret the decrease in urinary output during the 3 days after the administration of hydrochlorothiazide as a result of dehydration after an increase in diuresis rather than as a decrease in the therapeutic activity of the drug. The satisfactory results obtained with one dose of 50 mg. show that there is no need for increasing the dosage, and that hydrochlorothiazide is an effective oral diuretic which has no contradications.

Study of the Effects of Two Iminodibenzyl Derivatives on the Rigidity Caused by Parkinsonism: Imipramine or N-(Gamma-Dimethylaminopropyl)-Iminodibenzyl Hydrochloride, and RP 8307 or [Beta-(Hydroxyethyl-4″ Piperazinyl)-3″ Propyl]-5 Iminodibenzyl. J. Sigwald, D. Bouttier, C. Ramondeaud and others. Presse méd. 67:1697-1698 (Oct. 3) 1959 (In French) [Paris].

Seventeen patients with parkinsonism, who were receiving the usual treatment, were given imipramine and/or RP 8307 in an attempt to control their motor disorders. The usual treatment for parkinsonism was interrupted in only 2 patients and was replaced by either imipramine or RP 8307 or both (in successive periods of treatment). The results were compared and evaluated, and the patients' conditions were ascertained before instituting the new therapy and during and after the treatment with each preparation. Imipramine was given to 13 patients, of whom 12 continued also under the previous treatment and 1 received only the new medication. The disease was very severe in 3 patients, severe in 6, and rather severe in 4. The dosage of imipramine varied between 4 and 16 tablets, of 25 mg. each, daily, with an average dose of between 4 and 8 tablets. The results were very good in 1 patient, good in 5, fair in 3, and poor in 1. The patient who obtained very good results was a 63-year-old woman with rather severe parkinsonism, who was unable to perform any of the everyday activities. She was receiving 225 mg. of isothazine daily. After receiving 2 tablets of imipramine a day, her condition improved considerably, and she became capable of caring for herself regularly. Her improvement became still more pronounced when the dose of imipramine was increased to 4 tablets a day.

RP 8307 was given to 11 patients, of whom 4 had very severe and 7 had severe parkinsonism. The initial dose varied between 150 and 300 mg. daily, and in some cases was as high as 450 mg. Even with high doses there were no side-effects, but there was an optimal dose beyond which the effects diminished. The results were good in 5 patients and fair in 4; one patient showed slight improvement, and one was a failure. The condition of a 59-year-old man who was suffering from very severe parkinsonism and speech impediment was transformed by the administration of 400 mg. of RP 8307 daily. He became capable not only of performing everyday activities but also of speaking understandably. Interruption of the therapy caused a relapse at the end of 3 days, but reinstitution of the treatment again gave favorable results.

In 2 patients the treatment with an iminodibenzyl derivative was given alone, after interruption of the previous usual therapy. In one of them, treated with *imipramine*, the general condition improved, but not the tremor. In the other, treated with RP 8307, there was considerable improvement in the ability to perform everyday activities, but it was necessary also to add the usual antiparkinsonism treatment. Taking the study as a whole, therapy with RP 8307 was more satisfactory because of its more pronounced results and because of the absence of unfavorable reactions. Both iminodibenzyl derivatives have a symptomatic effect which persists only as long as the therapy is maintained, and both gave the 17 patients studied a relief of their motor disability which was not obtained with any other treatment.

The Supportive Effect of Glucocorticoids in Patients with Tuberculous Exudative Pleurisy. H. Brückner and G. Fiegel. Tuberkulosearzt 13:705-710 (Oct.) 1959 (In German) [Stuttgart, Germany].

The authors report on 18 patients with tuberculous exudative pleurisy, who were admitted to the Martins Hospital in Koblenz, Germany. They were given continued oral therapy with 10 mg. of isoniazid per kilogram of body weight and 15 to 30 mg. of prednisone/prednisolone; they received, in addition, intermittent instillations into the pleural cavity of a mixture of 60 mg. of prednisolone acetate (Deltacortril), 1 Gm. of streptomycin, and 250 mg. of a broad-spectrum antibiotic (to prevent an occasional mixed infection), at intervals of 6 days. Chest roentgenograms were taken every 6 days. In only 5 of the 18 patients were more than 2 instillations required at intervals of 6 days. In the other 13 patients, the reabsorption of the exudate had definitely started already after the first instillation, and complete disappearance of the exudate occasionally occurred after 12 to 18 days. In addition to rapid restoration of the erythrocyte sedimentation rate to normal, regression of lymphocytosis, and increased appetite and body weight, a surprisingly quick improvement of the general condition was noted. After reabsorption of the exudate, oral therapy with glucocorticoid and isoniazid was continued for 4 to 6 weeks, and the patients then were transferred to a sanatorium for treatment with isoniazid alone. There were no recurrences, and fibrous adhesions were not observed.

The brief duration of the disturbance of the general condition and the rapid improvement of the acute and often severe disease frequently made it difficult to impress on the patient the necessity of a subsequent sojourn in a sanatorium.

Hydrocortisone Sodium Succinate in Blood Transfusion: Pathogenetic and Therapeutic Contribution to Knowledge of the Chill-and-Fever Syndrome. C. M. Bianchi. Minerva chir. 14:1075-1081 (Sept. 15) 1959 (In Italian) [Turin, Italy].

The literature reveals that the chill-and-fever syndrome due to pyrogenic, allergic, or hemolytic cause occurs after the transfusion of blood with a 0.8 to 10% frequency. The author studied the effect of hydrocortisone sodium succinate therapy when given (1) before the transfusion in 68 patients, (2) during the transfusion in 10 patients, and (3) after the appearance of the syndrome in 22 patients. Each patient received an injection of 100 mg. of hydrocortisone sodium succinate. No untoward side-effects were observed in any of the patients who ranged in age from 2 to 75 years. A double dose, however, had to be administered to one patient. In the 22 patients of the third group the syndrome appeared, despite the fact that they had been given antihistaminic drugs before the blood transfusion. With the injection of hydrocortisone sodium succinate the chill disappeared in all the patients in 1 to 10 minutes, and the temperature became normal in 15 patients.

The author believes that hydrocortisone sodium succinate is useful in the prophylactic treatment of the postinfusional or the posttransfusional chill-and-fever syndrome. The pathogenetic mechanism of the chill-and-fever syndrome and the mechanism of action of the various drugs in preventing or resolving the syndrome are unknown. The author believes that the marked beneficial effect of hydrocortisone sodium succinate is due mainly to the glycogenetic effect of the drug. This study is a contribution to a better understanding of the role of the adrenal cortex in eliminating the severe condition of stress caused by the syndrome.

Infections During Treatment with Chlorpromazine and Perphenazine. E. Ose. Tidsskr. norske laegefor. 79:1119-1124 (Oct. 1) 1959 (In Norwegian) [Oslo].

The administration of phenothiazine compounds may cause a delay of healing in lung infections. Two cases of atypical pneumonia with more serious course originated during treatment with chlorpromazine and perphenazine respectively. Leukopenia is regarded as an absolute contraindication for treatment with chlorpromazine and perphenazine. Care should be exercised in application of phenothiazine treatment if the sedimentation reaction is increased, and the treatment should be discontinued at once if fever sets in. The finding of a "normal" number of leukocytes on perphenazine treatment does not seem to afford any assurance that the medication can be continued without risk if infection is suspected.

PATHOLOGY

A Clinical and Pathological Study of 63 Functioning Parathyroid Tumors. G. Kleinfeld. Cancer 12: 902-911 (Sept.-Oct.) 1959 [Philadelphia].

It is recognized that functioning parathyroid tumors may cause severe damage to the bones and kidneys, and surgical excision is the only effective treatment. Between 1906 and 1957, there were 63 accessions of functioning parathyroid tumors to the surgical pathology files of the Presbyterian Hospital, New York. Two tumors were functioning parathyroid carcinomas. This paper is concerned with data on 61 parathyroid adenomas in 59 patients, 2 of the adenomas being recurrent. The duration of symptoms ranged from 3 months to 25 years and averaged 6 years. All but 3 of the patients were between 20 and 59 years of age. No correlation could be established between histopathological findings and the clinical syndromes. There was, however, a relationship between preoperative serum calcium levels and tumor size, the adenomas becoming larger as the serum calcium level rose. Larger adenomas were found in patients with skeletal involvement than in those free of skeletal disease. The smallest adenomas were found in patients with calcium levels of less than 14 mg. per 100 cc. and exclusively renal involvement, these tumors usually being about 1 cm. in greatest dimension.

Inasmuch as the great majority of parathyroid adenomas are accessible through a standard low-collar incision, it is recommended that exploration of the mediastinum through a midline, sternal-splitting incision be postponed until after a fruitless exploration of the neck and upper mediastinum. The pathologist may then, at his leisure, carefully examine suspicious tissue fragments from the cervical region without risking the occasional diagnostic pitfalls of quick frozen section diagnosis. Should the examination prove negative, the mediastinal exploration may be undertaken as a separate procedure. However, the surgeon must not terminate the neck exploration without incision into, or partial excision of, the thyroid gland, in view of the significant incidence of adenomas embedded in the thyroid. In addition, all the parathyroids should be examined to insure against overlooking multiple adenomas. Exploration of the neck, in expert hands, carries very low operative mortality and morbidity rates and should be employed in patients who manifest advancing renal lithiasis. The adenomas in these patients, with minimally elevated serum calcium levels and renal disease without skeletal involvement, are very likely to be small, often less than 1 cm. in greatest dimension. The case of one of the 2 patients with functioning parathyroid carcinoma was unique in that a functioning, apparently solitary metastasis was excised after excision of the primary carcinoma, and total remission of the hyperparathyroid state resulted.

Paget's Disease of the Breast in Men: Case Report. J. B. da Silva Neto and H. Torloni. Rev. Assoc. méd. brasil. 5:257-259 (Aug.) 1959 (In Portuguese) [São Paulo, Brazil].

The authors describe the first case reported in Brazil of Paget's disease of the breast in men. The patient, a 55-year-old man, complained of eczema on the left nipple, of 20 years' duration. Radiation therapy received during the last 5 years had brought about some relief. At examination, the left nipple was found to have almost completely disappeared; its remnant was in the center of an extensive peripheral lesion, 8 by 2 cm., which was irregular in contour and reddish at some points. Palpation revealed a nodule, 2 by 1 cm., in the center of the cutaneous lesion. The clinical diagnosis of Paget's disease was established, and a radical mastectomy was performed. Macroscopically, no tumor was visible. The tissue subjacent to the nipple was thickened, especially at the nipple level where it had a 3-mm. thickness. The microscopic examination revealed malignant epithelial neoplasia, frankly intraductal. The epidermis was infiltrated with large tumor cells, and a lymphoplasmocytic infiltration was present along the subjacent chorion. Only 1 of the 27 lymph nodes removed was involved in the neoplastic formation, with invasion of the marginal sinus by neoplastic cells. The tumor was found only histologically; the glandular origin of the neoplasia was evident, although the primary tumor resembled an intraductal carcinoma.

Malignant Hypertension in a Case of Nonchromaffin Paraganglioma with a High Concentration of Catecholamine. G. M. Molinatti, F. Camanni and A. Pizzini. Cancer 12:878-883 (Sept.-Oct.) 1959 [Philadelphia].

Malignant hypertension due to abnormal secretion of catecholamine may be caused by tumors of the adrenal medulla and paraganglions. The cells of such tumors are characterized by an affinity for chrome salts. The staining with chrome salts is generally thought to be a true histochemical reaction that roughly measures the amount of catecholamine in the tissue. Chemical titration of catecholamines has constantly demonstrated the presence of large amounts of these hormones in chromaffin tissues. Hence, a tissue staining for chromaffin is generally considered as the site of a well-defined type of endocrine activity, while a lack of chromaffinity supposedly indicates an absence of catecholamines in the tissue. The authors present a 24-year-old woman who had a paraganglioma, severe symptoms of hypertension, and increased urinary excretion of catecholamine. The excision of the tumor, localized at the bifurcation of the aorta, resulted in the complete disappearance of the clinical symptoms. Histochemical examination of the paraganglioma showed a total absence of chromaffinity in the tumor tissue, while biological quantitation and chromatographic analysis showed a high concentration of catecholamines, especially arterenol. The finding of large amounts of catecholamines in a nonchromaffin paraganglioma, responsible for hypertension, has not so far been reported in the literature.

Histopathology of Pheochromocytoma. R. P. Sherwin. Cancer 12:861-877 (Sept.-Oct.) 1959 [Philadelphia].

The chromaffin reaction, structure, and problem of cancer are the 3 basic aspects in the tissue diagnosis of pheochromocytoma. The term "chromaffin positive" is often used in reference to tests other than the Henle dichromate reaction, but the author feels that substitute "chromaffin stains," such as Schmorl's, Gomori's, and the silver and osmium metalloreduction tests, when positive, are not pathognomonic of pheochromocytomas, whereas the Henle reaction is. Unfortunately, even the Henle reaction is not uniformly described, especially as regards its end-point, and the presence of brown granules has been overemphasized. Some distinctive morphologic features, on the other hand, have been neglected. The recognition of cancer in pheochromocytoma is difficult for several reasons.

Because of these problems, a total of 107 cases of pheochromocytoma from various sources were reviewed in reference to the Henle reaction, structure, and recognition of cancer. Forty-four cases were studied by subserial sections and multiple-staining procedures. A positive Henle reaction, with use of a thick section of fresh tissue, was found to be the most valuable aid in establishing the diagnosis. In cases in which the Henle reaction was questionable or not demonstrable because of Formalin fixation, certain morphologic features were emphasized as diagnostic aids. Since the cardinal clinical features of pheochromocytoma can be produced by many other conditions, strict attention to the pathological criteria should lead to greater accuracy in the diagnosis.

The incidence of malignant pheochromocytomas becomes much lower when cases with poor documentation are excluded. The rarity of malignant change of pheochromocytomas with the usual structure should favor a conservative resection when the tumor extends close to a kidney. A predominantly spindle-cell growth pattern occurred in the

3 malignant pheochromocytomas of this series and in many of the malignant pheochromocytomas reported elsewhere. A tendency toward isolated vertebral involvement by metastatic tumor is suggested.

A Case of Pulmonary Metastases from Carcinoma of Breast Successfully Controlled by Testosterone. D. K. Sambrook. Brit. J. Surg. 47:53-54 (July) 1959 [Bristol, England].

A lump developed in the upper inner quadrant of the left breast of a 36-year-old woman early in 1949. In September, 1949, she had local removal of the lump, which was found to be a scirrhous carcinoma of high-grade malignancy. It was decided to treat the breast and the regional glandular areas by deep roentgen-ray therapy without any further surgical treatment. A tumor dose of 4,000 r was applied in about 4 weeks. After the usual reaction the breast assumed a practically normal appearance, with only a small scar. The patient remained well until March, 1954, when she complained of a cough, and a roentgenogram of the chest showed several rounded opacities typical of pulmonary metastases.

The menopause was now induced by roentgen irradiation of the ovaries, and the woman was given 50 mg. of methyltestosterone by mouth twice a day, for a period of 2 months. At the end of this period she felt well, and a roentgenogram of the chest taken in June showed complete disappearance of the pulmonary metastases. In November, 1954, intramuscular injections of a testosterone preparation were begun, and were continued twice a week for 8 weeks. The patient remained well without signs of local recurrence for 3 years. A gynecologist, to whom she was referred in February, 1957, because of dyspareunia, prescribed estroform pessaries, which the woman inserted every night for about 10 days each month, until January, 1958, when she complained of pain in the scar in her breast. A palpable mass in the scar was excised. So far (April, 1959) no sign of further local recurrence has become evident.

It is remarkable that in this case metastases disappeared after only a few months' hormone treatment, and have not recurred more than 3 years later. It is also interesting that the tumor deposits in the lung were apparently unable to maintain their viability, whereas residual tumor cells in the breast must have done so.

***Our Experience with Puncture Biopsy* of Lymph Nodes.** G. Marchal, G. Duhamel and S. Perlès. Semaine hôp. Paris 35:2630-2631 (Oct. 4) 1959 (In French) [Paris].

The authors developed a technique for puncture biopsy of lymph nodes, as a diagnostic aid to simple puncture, whenever it is desirable to learn the structure of the lymph nodes and at the same time avoid the disadvantages of a surgical biopsy. This new technique utilizes Silvermann's bivalve trocar and consists in introducing the trocar guide into the lymph capsule under a light anesthesia. Pushed into the lymph pulp, the trocar cuts out a small cylindrical specimen, which is fixed on a slide and is treated by the usual histological methods.

Three cases are described. In a 46-year-old man, in whom a simple lymph node puncture had shown cells of malignant type, the puncture biopsy established the diagnosis of bronchial epithelioma. In a 69-year-old woman, in whom the simple puncture had shown large cells with light and nucleolated nuclei, the puncture biopsy established the diagnosis of a reticulosarcoma. In a 37-year-old man with lymphatic enlargement along the axillary line and an inconclusive simple puncture, the puncture biopsy showed lymphogranulomatous tissue typical of a polymorphous granuloma. In these 3 cases the puncture biopsy confirmed the suspicion which had been raised by the puncture. In other instances, such as in Brill-Symmers disease, Besnier-Boeck-Schaumann disease, and tuberculous lymphomas, the new technique, revealing the lymph node structure without its removal, is particularly useful for establishment of the diagnosis.

Ruptured Abdominal Aortic Aneurysm with Massive Gastrointestinal Hemorrhage. N. Kubota and V. Moragues. Am. Heart J. 58:547-555 (Oct.) 1959 [St. Louis].

To 63 previously reported cases of rupture of an abdominal aortic aneurysm, associated with gastrointestinal hemorrhage, the authors add 4. All 4 patients were men, ranging in age from 61 to 81 years; they all died, and autopsy was performed. In 3 of the 4 patients the rupture occurred directly into the third portion of the duodenum, and in the 4th case the rupture was into the intraperitoneal and retroperitoneal spaces, but there was no demonstrable communication between the lumen of the intestine and the aneurysm at autopsy. Discussing these 4 patients and literature reports, the authors point out that, with the declining incidence of syphilis and the increasing longevity of the population, arteriosclerotic aneurysms have become the commonest type. They usually occur in the abdominal aorta below the origin of the renal arteries. The occurrence of massive gastrointestinal hemorrhage caused by rupture of an abdominal aortic aneurysm is extremely rare. The most common site of rupture into the gastrointestinal tract has been the duodenum, particularly the third portion. The reason for this high incidence of rupture into the third portion of the duodenum is explained by the combination of anatomicomechanical relations. The third portion of the duodenum is relatively fixed because of its retroperitoneal position and its relation to the superior mesenteric artery, ligament of Treitz, aortic wall, and the vertebral column. Since these arteriosclerotic aneurysms of the lower abdominal aorta tend to bulge anteriorly over the course of time, these expansile pulsating masses can cause erosion, necrosis, and perforation of adjacent structures in much the same way as thoracic aneurysms do.

Attention is called to the fact that in a patient with a characteristic vascular crisis followed by gastrointestinal hemorrhage, in whom the history and findings indicate the presence of an abdominal aneurysm which has been painful or tender, the possibility of perforation of the aneurysm into the gastrointestinal tract must be considered. Surgical resection of the aneurysm and use of an arterial graft should be carried out. In the first of the 4 patients presented, surgical intervention should have been seriously considered after the first episode of hemorrhage, since the radiologist suggested the presence of an abdominal aortic aneurysm. In the 4th case, surgical exploration was withheld because of the questionable presence of an extensive thoracoabdominal aneurysm, which turned out to be 2 separate aneurysms. Surgery is the only lifesaving procedure even after the rupture of an aneurysm into the gastrointestinal tract, because this condition is uniformly fatal when left untreated.

Chemical and Pathological Studies on Aortic Atherosclerosis: A Comparative Study of One Hundred Twenty-Eight Aortas in South African Bantu and White Subjects. M. Anderson, A. R. P. Walker, W. Lutz and J. Higginson. A. M. A. Arch. Path. 68:380-391 (Oct.) 1959 [Chicago].

The authors determined the dry weight and concentrations of total ash, calcium, total lipid, cholesterol, phospholipid, nitrogen, elastin, collagen, and hexosamine in the aortas obtained from consecutive autopsies which were performed on 70 Bantu patients at the Baragwanath Hospital and on 58 white patients at the Johannesburg General Hospital, in Johannesburg, Union of South Africa. Before these determinations were made, the aortas had been graded for the degree of atherosclerosis. Mean total weight and lipid, cholesterol, and phospholipid concentrations showed definite correlation with the degree of atherosclerosis in both races. Ash and calcium concentrations showed a correlation in the aortas of white patients but not in those of the Bantu patients. Furthermore, in aortas of the same grade there were differences between the 2 races in regard to ash, calcium, and cholesterol concentrations. The differences were sufficiently large as to be not wholly explicable on the basis of subjective error in grading, and hence probably represent true qualitative differences in atherosclerosis, especially in regard to classification. However, there is evidence that considerable changes in chemical composition also occur with age within the same grade, thus obscuring the picture.

Differences in the concentrations of various chemical components, notably calcium, cholesterol, and hexosamine, were shown between Bantu and white persons, especially in the older decades. Further, the mean degree of atherosclerosis and total dry weight were significantly less in Bantu than in white persons. It is suggested, accordingly, that further racial studies should take into consideration qualitative, as well as quantitative, differences in the atherosclerotic processes. However, these racial differences, if representative of the degree of atherosclerosis and if equally applicable to the coronary artery system, would appear insufficient to explain the marked differences in the incidence of myocardial infarction shown by the 2 races.

Behavior of Thrombocytes in Patients with Hemophilia and in Female Conductors. A. Fonio. Schweiz. med. Wchnschr. 89:1026-1028 (Oct. 3) 1959 (In German) [Basel, Switzerland].

The author examined the morphologic and functional behavior of the thrombocytes in 31 patients with hemophilia and in 19 female conductors (transmitters of the hereditary trait). In contrast to the platelets obtained from normal persons, the onset of decomposition and of formation of fibrin occurs later in the platelets obtained from the hemophiliacs. On the 3rd day of observation in the dark field, and occasionally even on the 4th or 5th day, the thrombocytes of the hemophiliacs can still be sharply shown on the microphotograph; they are smaller, rounder, more sharply delineated, and brighter than the normal thrombocytes. The hemophilic thrombocytes are more resistant to decomposition than the normal platelets, and the discharge of thromboplastin as the product of secretion is delayed; from that the delayed and deficient coagulation in the hemophiliacs results. Concerning the functional behavior of the hemophilic thrombocytes, an additional defect has been observed, i. e., a pathological veil-like retraction of the plasma coagulum. In 18 of the 31 hemophiliacs, a marked veil-like retraction was found, and all these patients had severe hemophilia. In patients with mild disease, the veil-like appearance may be slight or absent.

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3 malignant pheochromocytomas of this series and in many of the malignant pheochromocytomas reported elsewhere. A tendency toward isolated vertebral involvement by metastatic tumor is suggested.

A Case of Pulmonary Metastases from Carcinoma of Breast Successfully Controlled by Testosterone. D. K. Sambrook. Brit. J. Surg. 47:53-54 (July) 1959 [Bristol, England].

A lump developed in the upper inner quadrant of the left breast of a 36-year-old woman early in 1949. In September, 1949, she had local removal of the lump, which was found to be a scirrhous carcinoma of high-grade malignancy. It was decided to treat the breast and the regional glandular areas by deep roentgen-ray therapy without any further surgical treatment. A tumor dose of 4,000 r was applied in about 4 weeks. After the usual reaction the breast assumed a practically normal appearance, with only a small scar. The patient remained well until March, 1954, when she complained of a cough, and a roentgenogram of the chest showed several rounded opacities typical of pulmonary metastases.

The menopause was now induced by roentgen irradiation of the ovaries, and the woman was given 50 mg. of methyltestosterone by mouth twice a day, for a period of 2 months. At the end of this period she felt well, and a roentgenogram of the chest taken in June showed complete disappearance of the pulmonary metastases. In November, 1954, intramuscular injections of a testosterone preparation were begun, and were continued twice a week for 8 weeks. The patient remained well without signs of local recurrence for 3 years. A gynecologist, to whom she was referred in February, 1957, because of dyspareunia, prescribed estroform pessaries, which the woman inserted every night for about 10 days each month, until January, 1958, when she complained of pain in the scar in her breast. A palpable mass in the scar was excised. So far (April, 1959) no sign of further local recurrence has become evident.

It is remarkable that in this case metastases disappeared after only a few months' hormone treatment, and have not recurred more than 3 years later. It is also interesting that the tumor deposits in the lung were apparently unable to maintain their viability, whereas residual tumor cells in the breast must have done so.

Our Experience with Puncture Biopsy of Lymph Nodes. G. Marchal, G. Duhamel and S. Perlès. Semaine hôp. Paris 35:2630-2631 (Oct. 4) 1959 (In French) [Paris].

The authors developed a technique for puncture biopsy of lymph nodes, as a diagnostic aid to simple puncture, whenever it is desirable to learn the structure of the lymph nodes and at the same time avoid the disadvantages of a surgical biopsy. This new technique utilizes Silvermann's bivalve trocar and consists in introducing the trocar guide into the lymph capsule under a light anesthesia. Pushed into the lymph pulp, the trocar cuts out a small cylindrical specimen, which is fixed on a slide and is treated by the usual histological methods.

Three cases are described. In a 46-year-old man, in whom a simple lymph node puncture had shown cells of malignant type, the puncture biopsy established the diagnosis of bronchial epithelioma. In a 69-year-old woman, in whom the simple puncture had shown large cells with light and nucleolated nuclei, the puncture biopsy established the diagnosis of a reticulosarcoma. In a 37-year-old man with lymphatic enlargement along the axillary line and an inconclusive simple puncture, the puncture biopsy showed lymphogranulomatous tissue typical of a polymorphous granuloma. In these 3 cases the puncture biopsy confirmed the suspicion which had been raised by the puncture. In other instances, such as in Brill-Symmers disease, Besnier-Boeck-Schaumann disease, and tuberculous lymphomas, the new technique, revealing the lymph node structure without its removal, is particularly useful for establishment of the diagnosis.

Ruptured Abdominal Aortic Aneurysm with Massive Gastrointestinal Hemorrhage. N. Kubota and V. Moragues. Am. Heart J. 58:547-555 (Oct.) 1959 [St. Louis].

To 63 previously reported cases of rupture of an abdominal aortic aneurysm, associated with gastrointestinal hemorrhage, the authors add 4. All 4 patients were men, ranging in age from 61 to 81 years; they all died, and autopsy was performed. In 3 of the 4 patients the rupture occurred directly into the third portion of the duodenum, and in the 4th case the rupture was into the intraperitoneal and retroperitoneal spaces, but there was no demonstrable communication between the lumen of the intestine and the aneurysm at autopsy. Discussing these 4 patients and literature reports, the authors point out that, with the declining incidence of syphilis and the increasing longevity of the population, arteriosclerotic aneurysms have become the commonest type. They usually occur in the abdominal aorta below the origin of the renal arteries. The occurrence of massive gastrointestinal hemorrhage caused by rupture of an abdominal aortic aneurysm is extremely rare. The most common site of rupture into the gastrointestinal tract has been the duodenum, particularly the third portion. The reason for this high incidence of rupture into the third portion of the duodenum is explained by the combination of anatomicomechanical relations. The third portion of the duodenum is relatively fixed because of its retroperitoneal position and its relation to the superior mesenteric artery, ligament of Treitz, aortic wall, and the vertebral column. Since these arteriosclerotic aneurysms of the lower abdominal aorta tend to bulge anteriorly over the course of time, these expansile pulsating masses can cause erosion, necrosis, and perforation of adjacent structures in much the same way as thoracic aneurysms do.

Attention is called to the fact that in a patient with a characteristic vascular crisis followed by gastrointestinal hemorrhage, in whom the history and findings indicate the presence of an abdominal aneurysm which has been painful or tender, the possibility of perforation of the aneurysm into the gastrointestinal tract must be considered. Surgical resection of the aneurysm and use of an arterial graft should be carried out. In the first of the 4 patients presented, surgical intervention should have been seriously considered after the first episode of hemorrhage, since the radiologist suggested the presence of an abdominal aortic aneurysm. In the 4th case, surgical exploration was withheld because of the questionable presence of an extensive thoracoabdominal aneurysm, which turned out to be 2 separate aneurysms. Surgery is the only lifesaving procedure even after the rupture of an aneurysm into the gastrointestinal tract, because this condition is uniformly fatal when left untreated.

Chemical and Pathological Studies on Aortic Atherosclerosis: A Comparative Study of One Hundred Twenty-Eight Aortas in South African Bantu and White Subjects. M. Anderson, A. R. P. Walker, W. Lutz and J. Higginson. A. M. A. Arch. Path. 68:380-391 (Oct.) 1959 [Chicago].

The authors determined the dry weight and concentrations of total ash, calcium, total lipid, cholesterol, phospholipid, nitrogen, elastin, collagen, and hexosamine in the aortas obtained from consecutive autopsies which were performed on 70 Bantu patients at the Baragwanath Hospital and on 58 white patients at the Johannesburg General Hospital, in Johannesburg, Union of South Africa. Before these determinations were made, the aortas had been graded for the degree of atherosclerosis. Mean total weight and lipid, cholesterol, and phospholipid concentrations showed definite correlation with the degree of atherosclerosis in both races. Ash and calcium concentrations showed a correlation in the aortas of white patients but not in those of the Bantu patients. Furthermore, in aortas of the same grade there were differences between the 2 races in regard to ash, calcium, and cholesterol concentrations. The differences were sufficiently large as to be not wholly explicable on the basis of subjective error in grading, and hence probably represent true qualitative differences in atherosclerosis, especially in regard to classification. However, there is evidence that considerable changes in chemical composition also occur with age within the same grade, thus obscuring the picture.

Differences in the concentrations of various chemical components, notably calcium, cholesterol, and hexosamine, were shown between Bantu and white persons, especially in the older decades. Further, the mean degree of atherosclerosis and total dry weight were significantly less in Bantu than in white persons. It is suggested, accordingly, that further racial studies should take into consideration qualitative, as well as quantitative, differences in the atherosclerotic processes. However, these racial differences, if representative of the degree of atherosclerosis and if equally applicable to the coronary artery system, would appear insufficient to explain the marked differences in the incidence of myocardial infarction shown by the 2 races.

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PUBLIC HEALTH

Staphylococcal Infection in Hospital Nurseries: Influence of Three Different Nursing Techniques. L. Frappier-Davignon, A. Frappier and J. St. Pierre. Canad. M. A. J. 81:531-536 (Oct. 1) 1959 [Toronto].

The authors conducted a field investigation in 26 hospitals, distributed throughout most of the districts of the province of Quebec, to determine the prevalence of staphylococcic infections in the nurseries and the influence on these infections of 3 important points of technique of infant nursing. Thirteen of the 26 hospitals fully met the requirements; of 16,053 births occurring in these 13 hospitals during 1956, there were 201 cases of staphylococcic infection which occurred in the nurseries, or an average incidence of 1.25% with a range of 0 to 4.7%, and this during a period when epidemics had abated. Layout and maintenance of the premises, space available for each infant, wearing of mask and gown, hierarchy and competence of the staff, method of examination of the infants by the physicians, and prohibition of admission of visitors and physicians in the nurseries were factors that were similar in all the hospitals. As the incidence of staphylococcic carriers was comparable in various nurseries with variable incidence of infection, this factor would not seem to have had much effect on the results reported here.

The outstanding differences among the hospitals related to the care of infants, particularly on the following 3 points: transferring the infants out of and into the nursery; scrub technique; and bathing of the newborn infant and products used to this end. The incidence of infection in hospitals in which all the infants, or only some of them, were transferred out of and into the nursery was very similar, namely, 1.5 and 1.9%. In contrast, in hospitals in which infants could on no account be taken out of the nursery, the incidence of infection was only 0.1%, or 10 or 15 times less. Furthermore, the results clearly showed that it makes no difference whether the infants are or are not bathed (with soap and water, oil, a proprietary preparation of 3% hexachlorophene, alcohol), provided that the infants do not leave the nursery and provided that the nurses and nursemaids wash their hands (soap, hexachlorophene) before handling each infant. Mere dipping of the hands in a parachlorometaxylenol (Det-tol) solution is equivalent to not washing them. On the contrary, it is far preferable to bathe the infants if they are transferred out of and into the nursery and/or if the personnel do not scrub. The influence of transferring the infants out of and into the nursery on the incidence of infection was studied for the first time in this investigation, and it may serve as a basis for a revision of the techniques followed in the care of infants in hospital nurseries.

Experimental and Epidemiologic Basis for the Interpretation of Tuberculin Sensitivity. C. E. Palmer, L. B. Edwards, L. Hopwood and P. Q. Edwards. J. Pediat. 55:413-429 (Oct.) 1959 [St. Louis].

It is accepted that nearly everyone who has had a tuberculous infection reacts to an intracutaneous test with the intermediate dose (0.0001 mg.) of purified protein derivative of tuberculin (PPD). Recent research indicates, however, that the reverse is not true. In some geographic areas, many of the reactions are not caused by tuberculous infection; they are cross-reactions, caused by natural infection with essentially nonpathogenic mycobacteria. The authors tried to produce in guinea pigs what they believe happens in human beings. Material for the present report was obtained as a by-product from a laboratory study on guinea pigs designed to investigate the virulence and the sensitizing and immunizing properties of the "Battey" mycobacterium.

Some of the animals were infected with virulent tubercle bacilli, and some with the nonphotochromogenic mycobacterium of the Battey type; some animals were not infected. Intracutaneous tests with standard mammalian tuberculin (PPD-S) and the PPD antigen prepared from the Battey organism (PPD-B) showed that, although cross-reactions occur with both types of infection, the homologous antigen usually produced a larger reaction than the heterologous antigen. Frequency histograms of the sizes of reactions to PPD-S for theoretical populations containing various proportions of tuberculous-infected, Battey-infected, and uninfected guinea pigs revealed patterns of sensitivity similar to those observed in human populations.

Parallel studies of patients in tuberculosis hospitals from whom only typical tubercle bacilli or Battey-type organisms had been recovered gave results like those found in the guinea pigs. Studies of healthy U. S. Navy recruits from different parts of the country, and of general population groups in this country and abroad, indicate that cross-reactions to tuberculin are highly prevalent in some geographic areas and much less prevalent in others; moreover, the frequency of cross-reactions varies with the prevalence of sensitivity to PPD-B. Whether the organism chiefly responsible for these cross-reactions is the Battey organism or some other related organism (or organisms) is still undetermined. It is clear, however, that when the frequency of tuberculin cross-reactions is high, and of specific tuberculous reactions is low, few of the tuberculous infected can be identified by the size of the tuberculin reaction alone. Simultaneous testing with PPD-S and other PPD antigens can then be expected to help determine the source of the tuberculin sensitivity, just as simultaneous testing with histoplasmin and coccidioidin helps to distinguish between the 2 fungous infections.

BOOK REVIEWS

Orthopædic Surgery. By Sir Walter Mercer, M.B., Ch.B., M.Ch.Orth. Fifth edition. Cloth. $12. Pp. 1075, with 422 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1959.

For those who have been Mercer fans over the years, this new edition will be a pleasure, as it is a useful mixture of the old and the new. The present-day student, however, and his house-officer colleagues may think it a bit old-fashioned. They will not be familiar, for instance, with the long rows of bedridden children on a sunlit porch getting nature's healing rays for skeletal tuberculosis, nor will they understand the emphasis on the symptoms and signs leading to a diagnosis of sacroiliac strain. They have been taught to be wary of the diagnosis of sacroiliac strain and to ascribe most of the troubles formerly thought of as sacroiliac to the lower lumbar elements. The chapter on congenital dislocation of the hip has been lengthened, and the basic features of this condition are well covered.

The longest treatise in the book is on tuberculosis of the skeletal system. It contains a wealth of material which attests to the professional lifetime interest of the author in this subject. He has reviewed and illustrated the old and presented in detail the modern concepts of treatment of the condition. Those methods he describes which are no longer in use in this country at least give us a historical background which should be part of our knowledge of any disease. The chapters on affections of the shoulder and knee are particularly enjoyable. For the guidance of those interested in studies of the knee there is an excellent figure depicting the normal medial and lateral meniscus in an air arthogram. The subject of sciatica presents the full impact of time and progress. In his 1936 edition, the author wrote one page about it; in 1959, he wrote 23 pages. This illustrates the recognition of the importance of the intervertebral disk.

Build and Blood Pressure Study, 1959. Volume 1. Paper. Pp. 268. Society of Actuaries, 208 S. La Salle St., Chicago 4, 1959.

This important book presents some of the results of an effort, in which 26 insurance companies cooperated, to determine the mortality of insured persons according to variations in body build and blood pressure. The questions ultimately to be answered are: "Just what are the optimum weights and heights for men and women at different ages?" and "How serious are the deviations from the assumed normal values of blood pressure at different ages?" An overwhelming mass of information was treated statistically. The conclusions about body build, for example, are based on a study of 4,900,000 insured persons, 133,000 of whom died.

The methods used in dealing with this mass of figures are described, the inaccuracies and limitations of the original data are discussed, and more than 124 tables are presented. This volume is primarily technical. The general medical reader will gain from it an appreciation of the difficulties encountered by a statistician in trying to make something out of such heterogeneous, not to say unreliable, data. What is he to do with weights "in indoor clothing," heights "in shoes," and blood pressures measured in noisy surroundings on applicants under tension? These and many other difficulties have been recognized, and the statistician has dealt with them as best he could, but it is evident that the value of the entire study would be immeasurably greater if the original data were not so poor. It is hoped that the concluding volume will spell out the conclusions to be drawn from this work. It will have to include explanations of some important terms like "ratable" and "fifth phase," which puzzle the reader since they are not listed in the index.

The investigation, monumental as it is, contains many only half-corrected errors and indicates many problems yet unsolved by statisticians. Future work of this sort should be based on physical measurements made by the examining physician on the spot with good apparatus. It is embarrassing to anyone concerned about the scientific status of this country to see weights recorded in pounds and quarters and heights given in feet, inches, and eighths; the long overdue shift to the metric system would not only make for more accurate data but would also save the statistician from the constant annoyance of dealing with inconvenient, antique units. It appears also that further standardization of sphygmomanometric procedure will be necessary if the figures given for normal states are to be reliable and their application to the individual patient is to be practicable. This volume is of interest to the physician mainly as a reminder that his contribution, his record of the results of a physical examination, largely determines the value of resultant statistical studies.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Open Reduction of Common Fractures. By Oscar P. Hampton, Jr., M.D., F.A.C.S., Assistant Professor, Clinical Orthopedic Surgery, Washington University School of Medicine, St. Louis, and William T. Fitts, Jr., M.D., F.A.C.S., Professor of Surgery, Schools of Medicine, University of Pennsylvania, Philadelphia. Modern surgical monographs. Editor-in-chief: I. S. Ravdin, M.D. Consulting editor: Richard H. Orr, M.D. Cloth. $8.75. Pp. 212, with 72 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1959.

This book, though small, is a gold mine of information. It has only three chapters: General Considerations, Fractures of the Upper Extremity, and Fractures of the Lower Extremity. In the last two chapters, every fracture which lends itself to open reduction and internal fixation is listed and the methods of performing the proper procedures are adequately described. In the first chapter many important points are brought up, such as the timing of the operation, technical principles of open reduction, special problems, and complications. Short, pithy paragraphs called "Pitfalls and Precautions" follow each section on a type of fracture.

This book deserves a place beside two other excellent small books: "The Closed Treatment of Common Fractures" by Charnley, and "Fractures in Children" by Blount. One might suggest that, as a minor criticism, in the case of subcapital fractures of the neck of the femur, the use of the Austin Moore pins or the Knowles pins as opposed to the Smith-Peterson nail was not sufficiently stressed. Furthermore, it was not suggested in the text or in the pictures that when the Smith-Peterson nail is used in fractures of the neck itself, a plate with screws should be attached to the outer end. One other small point is that it is clearly stated in the text that the Rush nail should be curved before it is used for fractures of the radius, but perhaps the nail should be used on the ulna only, that is, in the bilateral fractures. Some other form of fixation on the radius is more likely to keep the curve of the radius and prevent distraction of the ulnar fragments. This valuable book should be in the hands of everyone who expects to do this sort of work.

Therapeutic Electricity and Ultraviolet Radiation. Edited by Sidney Licht, M.D. Fourth volume of Physical Medicine Library. Cloth. $10. Pp. 373, with 94 illustrations. Elizabeth Licht, Publisher, 360 Fountain St., New Haven, Conn., 1959.

The mild surprise evoked by finding a new textbook on therapeutic electricity and ultraviolet radiation is in no way lessened by the following statement which appears in the preface: "Treatment with electricity and ultraviolet energy is diminishing as new remedies are discovered, but patients will continue to benefit from them for a long time to come." A rather rapid-fire history of electrotherapy based on some 920 references is contained in the first 69 pages of this book. Unfortunately, little or no attempt was made to separate advantages for which there is scientific evidence of their result from the therapy from those whose cause is unknown and those that obviously do not arise from therapy. Although replete with information of a historical nature, this section cannot be considered a guide to therapy.

The first two chapters of the succeeding section deal with apparatuses and techniques for electrical nerve-muscle stimulation. These chapters are well done, but the next two chapters are less commendable. The first chapter deals with the rapidly disappearing practice of iontophoresis, and the next is translated from the Russian and is about electrosleep, a procedure whereby a patient is put to sleep by currents applied to the head through electrodes. One electrode is placed over each eye and one over the occiput. No scientific data or reports of controlled studies are provided. Consequently, although the section provides interesting reading, the technique is difficult to evaluate.

The remainder of the text is concerned with ultraviolet therapy. In this part of the book, the history of ultraviolet therapy, methods of generation, indications for use, and techniques of treatment are discussed. The common sense and conservatism used in listing the conditions for which ultraviolet light may be used are gratifying to note. The volume does not hold that ultraviolet radiation is useful for the broad range of conditions that were formerly treated with it. The more discerning way of listing the conditions amenable to ultraviolet therapy is commendable. One cannot help but believe that if the text were to be rewritten 10 years from now, still fewer uses for this form of therapy would be listed.

Carcinogenesis By Ultraviolet Light. By Harold F. Blum. Cloth. $6.50. Pp. 340, with 58 illustrations. Princeton University Press, Princeton, N. J., 1959.

This is a readable description of important properties of ultraviolet rays and the mechanism of their carcinogenic action. Although the text is informative and detailed, it is also philosophical and contains speculative proposals. The first part of the book contains three chapters in which a good description is given of physical properties and of sources of ultraviolet rays. The significance of action and absorption spectrums is also discussed. This discussion includes a comparison of absorption with photochemical efficiency.

The second part covers the biological effects of ultraviolet rays. A mathematical formulation of these responses is presented. The inactivation of enzymes and viruses, hemolysis, and other phenomena are presented in detail. This part offers a relatively brief but pertinent comparison between the action of ultraviolet rays, visible light, and ionizing radiation. This comparison is given for a variety of phenomena, particularly with respect to oxygen-photorecovery. The process of normal cell division and the effect of ultraviolet light in its delay is lucidly outlined. Genetic and somatic mutations are described for both normal and neoplastic cells. This section ends with a discussion of the complex features of the absorption of ultraviolet light by skin.

The third part is devoted to descriptions of experimental data on carcinogenesis due to ultraviolet rays. Several experiments are described to elucidate the dependence of the effects on dose rate, wave length, and tumor type. Mathematical expressions for these data as related to the growth of tumor masses are evolved. A model is developed on the basis of an increasing number of clones whose rate of replication is constantly accelerated. This section ends with speculation concerning a postulated nucleic acid template as an ingredient in cell nuclei which controls the rate of proliferation.

The fourth part takes up human experience with cancer of the skin. The data are specifically analyzed with respect to correlation (1) of cancer with exposure of parts of the body to sunlight, (2) of incidence of skin cancer with regions of the earth having different amounts of sunlight, (3) with pigmentation, and (4) with outdoor and indoor occupations. The entire text is written lucidly so that, although complex and detailed processes are described, it is done in a most understandable way. For any clinician or biophysicist who desires an authoritative and stimulating presentation of fundamental considerations on this subject, this book is highly recommended.

Mitral Valvulotomy. By Harold J. Stewart, M.D., Professor Clinical Medicine, Cornell University Medical College, New York, and Frank Glenn, M.D., Lewis Atterbury Stimson, Professor of Surgery (chairman), Cornell University Medical College. Cloth. $10.50. Pp. 244, with 26 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

This book is enjoyable reading and is highly recommended to those who are interested in cardiac surgery or cardiology. It is an accurate and inclusive review of a series of patients who were operated on for mitral stenosis. It is an excellent guide for the selection of patients and the expected end-results from mitral valvulotomies as they were done in 1951, 1952, and 1953. Although the techniques have improved since then, this book is still a worthwhile addition to any cardiologist's or cardiovascular surgeon's library as a guide in evaluating patients with mitral valvular disease.

Part 1 deals exclusively with a review of the first 100 patients operated on by the authors in 1951, 1952, and 1953. This review includes their selection of patients, the type of operation done, the complications, and the end-results. Part 2 deals with the second and third 100 patients operated on during the years of 1954, 1955, and 1956. This review deals with the more widely used techniques, the use of additional information gleaned from the first 100 patients, and some of the complications encountered as a greater number of patients were operated on. Interesting incidental discoveries such as the high incidence of gallbladder disease associated with mitral stenosis are discussed. Part 3 covers the long-term follow-up examination of the general condition of the first 100 patients, the number dead among them, and the cause of their deaths. It also includes a follow-up study of the patients who required a second operation and indicates the type of valve encountered and the type associated with the longest satisfactory functional status.

Although the technique of mitral valvotomy has changed and will change from that which was performed in this group of patients, this book remains an important adjunct in the literature of cardiovascular surgery and should be of great value to those physicians who are actually engaged in the problem of evaluating and following up patients who have had mitral valvotomy. It probably has limited value for the intern or medical student. It is well organized and is easily read.

A Text-Book of X-ray Diagnosis. In Four Volumes. Volume IV. By British authors. Edited by S. Cochrane Shanks, *C.B.E.*, M.D., F.R.C.P., F.F.R., Director, X-ray Diagnostic Department, University College Hospital, London, and Peter Kerley, *C.V.O.*, *C.B.E.*, M.D., F.R.C.P., F.F.R., Director, X-ray Department, Westminster Hospital, London. Third edition. Cloth. $21. Pp. 714, with 735 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England; H. K. Lewis & Co., Ltd., 136 Gower St., London, W. C. 1, England, 1959.

It is difficult to review a book which provides so little for adverse criticism. This volume, now in its third edition, is one of four covering the entire field of roentgenographic diagnosis on an encyclopedic scale. The authors have enlarged this volume with 291 additional pages and 249 illustrations reflecting the enormous advances in the field since the last edition in 1950. The subject matter has been divided into 11 parts covering in a comprehensive manner all phases of the roentgenographic diagnosis of bone and joint diseases and including a section on localization of foreign bodies. The descriptions are concise, easily readable, and always adequate and include useful data about cause, lesions, clinical features, and often technical aspects. The illustrations are well chosen. Not only are the pathological changes considered but also the normal variants of bone development are fully described and illustrated.

This volume with the other three provides an encyclopedic coverage of the entire field of roentgenographic interpretations and have long been accepted as classics by English-speaking physicians. These textbooks from the first printing have enjoyed well deserved success and popularity. This third edition should receive the same enthusiastic acceptance. This particular volume is enthusiastically recommended not only for the graduate student in radiology, his preceptor, and all radiologists but also for the orthopedist and any physician interested in bone and joint disease.

Principles of Disability Evaluation. By Wilmer Cauthorn Smith, M.D. Cloth. $7. Pp. 210. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada; Pitman Medical Publishing Company, Ltd., 39 Parker St., London, W. C. 2, England, 1959.

The vast experience of Dr. Smith, including many years as a member of the Oregon State Industrial Accident Commission, makes this volume especially valuable. The ever-increasing interest of the medical profession in the evaluation of injury should be further clarified by this book, which is divided into four main sections, each dealing with different phases of disability evaluation. These may well assist the novice as well as the experienced evaluator. The introductory section, dealing with the general concepts of disability, points out the role of the physician and his limitations. There is presently operating in this field a committee of the American Medical Association which works closely with social security authorities in establishing criteria of impairment. The trend is toward the evaluation, by physicians, of impairment rather than disability.

The second section covers general as well as specific instances and again clarifies the physician's relationships. The association and relationship of injury and disease to disability are brought out in the third section. In the final section examples of scheduled and nonscheduled injuries, and of patients with several disabilities, especially with those of the extremities, are presented. This contribution to an ever-growing field is recommended to all physicians interested in this subject. There can be no substitute for experience. Dr. Smith has wide knowledge of this subject, and he presents his thoughts capably and clearly.

Doctors and Patients: Stories by Leading American Physicians. Edited by Noah D. Fabricant, M.D. Half cloth. $5.25. Pp. 204. Grune & Stratton, Inc., 381 Park Ave. S., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1959.

This book consists of a collection of 31 short contributions by various distinguished physicians. None of the items are so long that they could possibly weary a reader or outlast his curiosity. The personalities revealed are as diversified as could be imagined, and the contributors are outstanding contemporaries whose items can hardly fail to interest innumerable friends and admirers. Some items breathe a wonderful warmth of human understanding while others are marked by a certain scholarly formality; one describes the cold reception of a stranger in a medical school full of climbers while another pictures the cordial welcoming, with horse-drawn carriages and a squadron of hussars, of American students to the Munich of 1912. Some of these items deserve to become classics—one a narrative of the unexpected results of restoring vision to the blind, another the account of the girl in Escanaba whose temperature had been reported as 114 F, and especially a third, entitled "It Wasn't Meant to Hurt." For the reader who loves to see the deflation of pompous or sadistic professors there are some hilarious stories naming places and people. This book is especially recommended to medical and premedical students as a kind of preview of the situations in which they are likely some day to find themselves.

The Surgical Treatment of Scoliosis. By Louis A. Goldstein, M.D., F.A.C.S., Associate Clinical Professor of Orthopaedic Surgery, University of Rochester Medical Center, Rochester, New York. Appendix: Anesthesia in Scoliosis by D. Vernon Thomas, M.B., F.F.A.R.C.S., Professor of Anesthesia, University of Rochester Medical Center. Publication number 345, American Lecture Series, monograph in Bannerstone Division of American Lectures in Orothopaedic Surgery. Edited by C. W. Goff, M.D., Associate Clinical Professor of Orthopaedics, Yale University, School of Medicine, Hartford, Conn. Cloth. $6.75. Pp. 116, with 47 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The author of this monograph has reviewed the previous and current thought on the treatment of scoliosis, both conservative and surgical. The book is based on the result of the surgical treatment of 65 patients, all treated in essentially the same manner. The technique of applying a Risser turnbuckle cast is described in sufficient detail to enable any orthopedist to apply a creditable cast. The surgical fusion is performed through a window in the cast, a technique which is being abandoned in many orthopedic centers as unnecessary and dangerous. The use of sharp gouges with hand pressure only is a point of technique that needs emphasizing, as it certainly minimizes surgical shock. The author, who has performed all of these spine fusions, is to be commended because only 13% of them resulted in pseudarthrosis. This points up the fact that a good fusion technique, adhering to proved principals, should yield a high rate of solid spine fusions. Many of the author's cases are illustrated in detail and should be instructive to any student of scoliosis.

A short section on anesthesia for scoliotic spine fusions by Dr. D. V. Thomas is included at the end of the book. All patients operated on in corrective casts are intubated with some difficulty because of the restrictions of the cast, but this essential step provides adequate oxygenation and adequate control of the depth and rate of anesthesia. The book is recommended to any serious student of the scoliotic spine.